

EXHIBIT 1

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

IN RE: VALSARTAN, : MDL NO. 2875
LOSARTAN, AND :
IRBESARTAN PRODUCTS : HON. ROBERT
LIABILITY LITIGATION : B. KUGLER

THIS DOCUMENT APPLIES :
TO ALL CASES :

- CONFIDENTIAL INFORMATION -
SUBJECT TO PROTECTIVE ORDER

September 14, 2021

VOLUME I

Videotaped remote deposition of LEE-JEN WEI, Ph.D., taken pursuant to notice, was held via Zoom Videoconference, beginning at 9:08 a.m., on the above date, before Michelle L. Gray, a Registered Professional Reporter, Certified Shorthand Reporter, Certified Realtime Reporter, and Notary Public.

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Testimony of:

LEE-JEN WEI, Ph.D.

By Mr. Nigh 12

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Direction to Witness Not to Answer

PAGE LINE

None.

Request for Production of Documents

PAGE LINE

None.

Stipulations

PAGE LINE

None.

Questions Marked

PAGE LINE

None.

1 - - -

2 THE VIDEOGRAPHER: We are
3 now on the record. My name is
4 Judy Diaz. I am a legal
5 videographer for Golkow Litigation
6 Services.

7 Today's date is
8 September 14, 2021, and the time
9 is 9:08 a.m.

10 This remote video deposition
11 is being held in the matter of
12 Valsartan, Losartan, and
13 Irbesartan Products Liability
14 Litigation MDL.

15 The deponent is Lee-Jen Wei
16 Ph.D.

17 All parties to this
18 deposition are appearing remotely
19 and have agreed to the witness
20 being sworn in remotely.

21 All counsel will be noted on
22 the stenographic record.

23 The court reporter is
24 Michelle Gray and will now swear

1 in the witness.

2 - - -

3 ... LEE-JEN WEI Ph.D.,
4 having been first duly sworn, was
5 examined and testified as follows:

6 - - -

7 EXAMINATION

8 - - -

9 BY MR. NIGH:

10 Q. Good morning. My name is
11 Daniel Nigh, and I represent the
12 plaintiffs.

13 Dr. Wei, could you please
14 state and spell your name, your last
15 name?

16 A. Name is W-E-I, Wei. First
17 name Lee-Jen, L-E-E, hyphenation, J-E-N.

18 Q. Okay. Let's take a look at
19 LP-1556.

20 (Document marked for
21 identification as Exhibit
22 Wei-1.)

23 BY MR. NIGH:

24 Q. That's how I'm going to call

1 them out, Doctor. And then the
2 videographer is growing to put the
3 document up on the screen. This will be
4 marked as Exhibit -- Exhibit 1.

5 Okay. This is -- Doctor,
6 this is your deposition here. Have you
7 seen this before today?

8 A. Yes, sir. Would you mind
9 blow up a little bit?

10 Q. Sure.

11 A. Thank you. Yeah. Thank
12 you.

13 Q. Yeah. And let's take a look
14 at the third page where it shows exhibit.
15 And let's go ahead and blow up document
16 requests, and the first couple -- the
17 first couple requests.

18 Do you see this here? On
19 the third page of this deposition there
20 was an attachment called exhibits.

21 Do you see this?

22 A. Yes, sir.

23 Q. And did you review this
24 request for exhibits -- or request for

1 documents I mean?

2 A. Yes, I did, with the lawyer.

3 Q. And you provided all of the
4 documents that you had that were
5 responsive to this to your lawyer?

6 A. As much as I can.

7 Q. Okay. Let's take a look at
8 LP-1600.

9 (Document marked for
10 identification as Exhibit
11 Wei-2.)

12 MR. NIGH: This will be
13 marked as Wei Exhibit Number 2.

14 BY MR. NIGH:

15 Q. Let's blow up the first part
16 of this. It says, "Defendants' responses
17 and objections to plaintiffs' notice of
18 videotaped deposition."

19 Do you see that?

20 A. Yes.

21 Q. And let's take a look at the
22 second page. Here we ask for copies of
23 all invoices. Let's look at Number 1,
24 the documents.

1 "Copies of all invoices" --
2 right at the very beginning -- "for work
3 performed in connection with any
4 consultation or expert work provided for
5 on behalf of any defendant."

6 Do you see that?

7 A. Yes, sir.

8 Q. And on the second page,
9 there are some objections.

10 The second page says,
11 "Subject to" -- or the next page says,
12 "Subject to" --

13 MR. NIGH: If we can blow
14 that part up.

15 BY MR. NIGH:

16 Q. "Subject to and without
17 waiving these objections and any of the
18 foregoing general objections, defendants
19 will produce invoices in advance of
20 Dr. Wei's deposition."

21 Do you see that?

22 A. Yes, sir.

23 Q. Okay. Do you believe that
24 you provided all of your invoices for

1 this case?

2 A. Yes. There is only one
3 invoice.

4 Q. Okay. Let's take a look at
5 the second request. It says, "Copies of
6 any notes, written or electronic,
7 reflecting consulting or litigation work
8 that has not been documented in
9 invoices."

10 A. Well, the only thing I have
11 is a draft of my report. So that's about
12 it.

13 Q. Okay. All right. Let's
14 take a look at Number 3.

15 Let me ask you this, when
16 you would be reviewing -- when you would
17 review literature articles, would you
18 keep notes on those literature articles
19 or would you keep notes anywhere, like in
20 a Word document?

21 A. No, sir.

22 Q. So you would only put your
23 notes into the draft of the report?

24 A. Sometimes I just highlight

1 the papers I'm reviewing.

2 Q. You would only highlight
3 papers that you're reviewing, but you
4 wouldn't write anything on those papers?

5 A. I don't think so for this
6 case.

7 Q. Okay. Number 3 says,
8 "Copies of any notes or other
9 documentation, including PowerPoints for
10 any presentations, seminars, or classes
11 given by Dr. Wei with regard to the risks
12 and benefits of any angiotensin blockers
13 or nitrosamines."

14 Did you have any notes or
15 other documentation for any
16 presentations, seminars, or classes --

17 A. No, sir.

18 Q. -- regarding ARBs or
19 nitrosamines?

20 No? Okay.

21 Do you recall giving any
22 presentations for ARBs or nitrosamines?

23 A. No, sir.

24 Q. Okay. Taking a look at

1 Page 4 -- Number 4. Sorry.

2 "Copies of any documents or
3 articles relied upon for the opinions set
4 forth in the report served."

5 At the bottom it says,
6 "Subject to and without waiving these
7 objections and any of the foregoing
8 general objections, defendants will
9 produce a copy of all electronically
10 available documents identified on
11 Dr. Wei's list of materials considered
12 prior to his deposition."

13 Did you also provide the
14 highlighted studies, studies that you
15 would put -- that you would highlight to
16 your attorneys?

17 A. Yeah, I remember I send two
18 articles with highlighted portions to the
19 lawyers.

20 Q. Are there only two articles
21 that you ever highlighted?

22 A. Yeah, pretty much.

23 Q. Okay. What are those two
24 articles?

1 A. I don't remember. I send it
2 to the lawyers last week.

3 Q. Okay. Let's take a look at
4 Number 5. "Copies of any documents or
5 articles reviewed in connection with the
6 report thereto, whether or not listed in
7 the report."

8 And the answer at the end
9 says, "Subject to and without waiving
10 these objections and any of the foregoing
11 general objections, defendants will
12 produce a copy of all electronically
13 available documents identified on
14 Dr. Wei's list of materials considered."

15 How did you pull together
16 your -- these electronic documents?
17 What's the process that you undertook to
18 pull these together in order to respond
19 to these requests?

20 A. Well, first, I got a list of
21 references that are recommended by the
22 lawyers. And I downloaded to my
23 computer, and as a PDF file. And
24 that's -- from there, I just used that

1 copies and reviewed papers, documents and
2 et cetera.

3 Q. Okay. So I think you said
4 you got a list of references from the
5 lawyers?

6 A. Yeah. It is a listing. It
7 actually is all the files. They send me
8 a website. I can just download it
9 easily.

10 Q. Okay. Was that like a
11 DropBox or some kind of platform where
12 you could download studies and internal
13 documents, that sort of thing from that
14 file?

15 A. Probably it's like a
16 DropBox. It's very convenient, actually.
17 I find it very nice.

18 Q. Okay. And is that where you
19 pulled all of your literature that you
20 reviewed in this case?

21 A. Yes.

22 Q. Okay. So all the literature
23 that you reviewed in connection with your
24 report was provided to you by the defense

1 attorneys?

2 A. Yeah. There's only one
3 thing that I did make a quick search
4 through the Google about other studies
5 directly related to impurity of valsartan
6 product.

7 Q. Did you find any additional
8 documents that you reviewed with that
9 Google search?

10 A. I did not.

11 Q. Okay. So if I understand
12 this correctly, you did a quick Google
13 search looking for anything related to
14 the impurity of the valsartan product,
15 and you didn't find any additional
16 documents that you reviewed with that
17 Google search, correct?

18 A. That's correct, sir. If I
19 may just add in one sentence. For all
20 other studies, publications, when I read
21 Dr. Madigan's report, if Dr. Madigan is
22 citing some reference or publication, was
23 not on the list, I would ask the lawyer
24 to send to me. That's what I did once to

1 the lawyer.

2 Q. Okay. So if I understand
3 you correctly, you also looked at
4 Dr. Madigan's report, and there was one
5 study that you didn't see in that DropBox
6 that you asked the defense lawyers to
7 provide to you?

8 A. Correct.

9 Q. Okay. So all of the
10 literature that you reviewed was provided
11 to you by your lawyers, correct? I mean,
12 by the defense lawyers, correct?

13 A. Yes.

14 Q. Okay. Let's take a look at
15 Number 6. "Any illustrations,
16 PowerPoints, images, charts, tables or
17 demonstrative exhibits that may be used
18 by or with Dr. Wei in connection with the
19 Daubert hearing or trial testimony in
20 this litigation."

21 Other than what's contained
22 in your expert report, you don't have any
23 other illustrations, PowerPoints, images,
24 charts or tables or demonstrative

1 exhibits that you're expecting to use,
2 correct?

3 A. Not yet.

4 Q. Not yet?

5 A. Yeah, so I think in my
6 report I clearly state that maybe in the
7 future we may actually create a
8 PowerPoint presentation or tables or
9 graphic display.

10 Q. Do you have any idea what
11 those tables or graphic displays would
12 look like --

13 A. No.

14 Q. -- at this time? No?

15 A. Not yet.

16 Q. Okay. So you understand
17 that I would have no ability to question
18 you regarding those demonstrative tables
19 or those charts here today if they're not
20 contained in your expert report and you
21 don't even know what they would be,
22 correct?

23 A. They don't exist yet.

24 Q. Right. So I wouldn't have

1 ability today to ask you questions today
2 regarding those charts or tables,
3 correct?

4 A. Fair enough.

5 Q. I'm sorry. What was your
6 answer?

7 A. I said fair enough. What
8 you're saying, yes.

9 Q. Okay. Let's take a look at
10 Number 7. Number 7, "Documentation of
11 any research grant the witness has been
12 provided to study any angiotensin
13 blockers, nitrosamines, and health
14 effects possibly related thereto."

15 You haven't received any
16 research grants related to ARBs, correct?

17 A. Correct.

18 Q. And you haven't received any
19 research grants related to nitrosamines,
20 correct?

21 A. Correct.

22 Q. Okay. Take a look at Number
23 8. "Documentation" -- "Documentation of
24 any research the witness has performed

1 with regard to any ARB or nitrosamine."

2 You haven't done any
3 independent research -- other than in
4 connection with your expert opinions here
5 today, you haven't done any independent
6 research regarding ARBs or nitrosamines,
7 correct?

8 A. Sir, let me make sure. This
9 is a pretty broad question. For the
10 safety or impurity of valsartan, I
11 haven't done anything except this report.

12 But if you're talking about
13 in general, the research regarding the
14 ARB, I did know something about it
15 because I work closely with Brigham and
16 Women's Hospital at Harvard cardiologists
17 for many years.

18 Q. Okay. Have you performed
19 research related to ARBs?

20 A. I believe in some of my
21 papers, I utilize some research papers
22 regarding to ARB, ACE inhibitor, beta
23 blockers in the past.

24 Q. Okay. Have you done any

1 research regarding nitrosamines?

2 A. I don't think so.

3 Q. In terms of ARBs, what would
4 be the extent of your research?

5 A. Well, mostly we are really
6 interested into combining ARB and ACE
7 inhibitor, see if we can get a better
8 treatment effect from this combination
9 compared with monotherapy, for example
10 ACE inhibitor or ARB alone.

11 Q. Other than measuring whether
12 or not you would get a better effect when
13 combining ARB and ACE inhibitor compared
14 to ACE inhibitor or ARB alone, have you
15 done any other research regarding ARBs?

16 A. I don't know exactly. But
17 sometimes I writing for physical papers,
18 I may cite it in some papers related to
19 ARB publications, mostly related to
20 efficacy. For example, reduced the
21 hospitalization, reduced the
22 cardiovascular death. That's most of my
23 statistical papers are about.

24 Q. Okay. If I understand you

1 correctly, you have cited to papers and
2 ARB publications, in large part as ARBs
3 are medications taken for hypertension
4 and help to reduce hospitalizations and
5 reduce cardiovascular death; is that
6 correct?

7 A. Yes, sir, for heart failure
8 patients. Mostly for heart failure, not
9 for blood pressure problem.

10 Q. Mostly for heart patients?

11 A. Heart failure.

12 F-A-I-L-U-R-E.

13 Q. Oh, heart failure. Okay.

14 And in terms of those
15 patients, if they were to stop taking
16 their ARB without any substitute, then at
17 the time that they're stopped taking the
18 ARB without any substitute, they would
19 lose the benefit of it helping to reduce
20 hospitalizations, reduce cardiovascular
21 death, correct?

22 A. I don't know. I'm not a
23 clinical person. I cannot make -- either
24 way.

1 Q. Let's take a look at nine.

2 Nine asked for, "Copies of
3 any documents, including protocols or
4 information about medication side
5 effects, available to the witness from
6 any hospital or academic institution
7 where he has worked, had an appointment,
8 or had privileges which set forth
9 information related to the risks and
10 benefits of any ARB or nitrosamine."

11 Do you see that?

12 A. Yes, sir.

13 Q. Now, you didn't have any
14 copies of documents, including protocols
15 or information about medication side
16 effects, correct?

17 A. I don't.

18 Q. Okay. Number 10, "Any
19 documents or other communications the
20 witness has received from any person or
21 entity with regard to nitrosamine
22 impurities in any ARB or other drug.

23 So other than the
24 documentation provided to you by your

1 counsel, you didn't have any other
2 documents or review any other documents
3 from any other person or entity regarding
4 nitrosamine impurities in ARBs, correct?

5 A. That's correct, sir. The
6 only thing that I'm really concerned is
7 about all the publications, documents
8 cited by Dr. Madigan in his report.

9 Q. Okay. Number 11, "Any
10 communications from the witness to any
11 person or entity with regard to
12 nitrosamine impurities in any ARB or
13 other drug, outside of communications
14 through counsel."

15 So other than -- other than
16 defense counsel, you haven't had any
17 other communications with any other
18 witness or any other person regarding
19 your work here regarding nitrosamine
20 impurities and ARBs, correct?

21 A. Correct.

22 Q. Okay. Number 12, "Any
23 textbook referenced by the witness in
24 forming his opinions."

1 You didn't rely on -- did
2 you rely on any portion of any textbook
3 to form your opinions here today?

4 A. Yes, sir. There is one
5 book --

6 Q. Which?

7 A. -- by David DeMets, Clinical
8 Trials. I cited in my report.

9 Q. Which textbook was that
10 again?

11 A. Do you have a list of
12 references? I can point it to you.

13 Q. We'll come back to that.

14 A. Furberg. I think the first
15 author is if Furberg, I think.

16 Q. We can take this down.
17 We'll take a look at your expert report.

18 This is LP-1557.

19 (Document marked for
20 identification as Exhibit
21 Wei-3.)

22 MR. NIGH: This will be
23 marked as Exhibit Wei-3.

24 BY MR. NIGH:

1 Q. Do you see this here? This
2 appears to be your expert report that you
3 prepared for this litigation, correct?

4 A. Yeah. May I see my
5 signature, on -- toward last -- if you
6 don't mind.

7 Q. Sure. Let's take a look at
8 Page 24.

9 A. Yes, sir.

10 Q. Is that your signature?

11 A. Yes, sir.

12 Q. The date of this is
13 August 2, 2021, correct?

14 A. Yes, sir.

15 Q. Now, you understand that one
16 of the purposes of this expert report is
17 to put us on the other side, you know, on
18 the plaintiffs' side, plaintiffs'
19 counsel, on notice of your opinions,
20 correct?

21 A. Yes, sir.

22 Q. And if you don't include
23 certain opinions in this expert report,
24 then we would not be provided notice of

1 those opinions, correct?

2 A. I don't know. Whatever you
3 say. I don't understand the rules
4 anyway, so I leave it up to you.

5 Q. Okay. Let's take a look at
6 Number 11 on Page 5. And this says
7 "Assignment."

8 And under assignment, it
9 says, "I have been retained by defendants
10 to provide an expert opinion in the
11 litigation styled In Re Valsartan
12 Products Liability Litigation.
13 Specifically, I was asked by counsel for
14 defendants to review and assess the
15 opinions presented by David Madigan,
16 Ph.D., who submitted an expert report on
17 behalf of plaintiffs analyzing the
18 results from the Dietary and Occupational
19 Studies to infer potential risk of
20 carcinogenicity of ND" -- I think you
21 meant NDMA, as opposed to NDME, right?

22 A. Yes. It should be NDMA.

23 Q. Okay.

24 -- "of NDMA or NDEA

1 impurities in valsartan and to provide my
2 own assessment of those issues."

3 Correct?

4 A. Yes, sir.

5 Q. Okay. And so is it your
6 understanding -- did you only become
7 involved after Dr. Madigan had completed
8 his expert report?

9 A. I believe so. I got
10 Dr. Madigan's report from the lawyer.

11 Q. Okay. And so when you
12 started, you had a completed report by
13 Dr. Madigan, correct?

14 A. Correct.

15 Q. Now, this isn't the first
16 time that you've been on the opposite
17 side of Dr. Madigan, correct?

18 A. It's the first time, you're
19 saying, sir?

20 Q. Right. This isn't the first
21 time. This is not the first time you've
22 been on the opposite side of Dr. Madigan,
23 correct?

24 A. No. I don't know how many

1 times.

2 Q. Okay.

3 A. I don't recall how many
4 times we were on opposite sides.

5 Q. Well, that's what I'm about
6 to ask you. What are the other times --
7 what other litigation can you remember
8 being on the opposite side of
9 Dr. Madigan?

10 A. I believe at least we had
11 Celebrex --

12 Q. Okay.

13 A. An injury case, and also
14 security case. Dr. Madigan was on the
15 wrong side. And I'm sorry. That's not
16 politically correct. I just -- he is on
17 the plaintiff's side.

18 Then you have Taxotere case
19 still ongoing. Dr. Madigan is on the
20 opposite side.

21 I believe there are other
22 cases, sir. I just don't remember.

23 Q. So the ones that you can
24 remember -- I'll make sure that I've got

1 this correctly. The ones that you can
2 remember that you've been on the opposite
3 side of Dr. Madigan, there's Taxotere
4 which is -- that's a litigation that's
5 still ongoing, correct?

6 A. Correct.

7 Q. There's Celebrex. Now,
8 that's a litigation that you got involved
9 in more than ten years ago, correct?

10 A. Yeah. Correct.

11 Q. You said there's a
12 securities case?

13 A. Yeah, it's actually economic
14 loss, in some way. This -- the investor,
15 they claimed they lost the money,
16 whatever it is, because the safety issue
17 about Celebrex.

18 Q. I see. Okay. And other
19 than those three, I think you mentioned
20 one or two more. What were the other
21 two -- or the other ones?

22 A. No, I -- I don't remember
23 other. I don't remember, sir.

24 Q. I see. So you just remember

1 those three?

2 A. Yeah, that's as far as I can
3 tell. But, you know, maybe there are
4 more.

5 Q. Okay. Now, who first
6 reached out to you in this case?
7 Which -- how was that contact made to
8 you?

9 A. It's defendant lawyers.

10 Q. Okay. Defending lawyers.
11 Which defending lawyer reached out to
12 you?

13 A. Steve -- Steven, right?
14 Steven.

15 Q. Steve Harkins?

16 A. Yeah. Hartley.

17 Q. Okay. So Steve Harkins
18 reached out to you?

19 A. Yes, sir.

20 Q. Have you ever worked with
21 Steve Harkins on any other litigation?

22 A. No, sir.

23 Q. Okay. All right. Let's
24 take a look here. You were asked to

1 analyze the opinions by Dr. Madigan. And
2 so a lot of your report will be basically
3 a response or criticism of Dr. Madigan's
4 report, correct?

5 A. Yes, sir.

6 Q. And then you put, "and to
7 provide my own assessment of those
8 issues."

9 Do you see that?

10 A. Yes, sir.

11 Q. Now, what do you mean --
12 other than responding or criticizing
13 Dr. Madigan, what did you do in terms of
14 providing your own assessment?

15 A. For example, I made a
16 comment about observational studies
17 issue. And I provide the valsartan
18 studies. And Dr. Madigan didn't mention
19 it at all in his report.

20 Q. Okay. So those are a couple
21 of examples where you say you made a
22 comment about observational study. And
23 then you reviewed the valsartan studies
24 and gave commentary on the valsartan

1 studies, right?

2 A. Yes, sir.

3 Q. Other than those two
4 examples, is there any other original
5 work that you did that wasn't just a
6 response or criticism to Dr. Madigan's
7 report?

8 A. Well, Counsel, if you don't
9 mind, maybe later on we can go through my
10 report. We probably can pick up
11 something I can share with you what are
12 the -- actually from my own opinions,
13 which are not. But right now, that's the
14 only two things that I remember.

15 Q. Okay. And we will go
16 through them further. I'm just trying
17 to, you know, lay some structure here
18 first.

19 So other than those two,
20 those are the only two opinions that you
21 can think of that are original opinions
22 as opposed to responding to Dr. Madigan?

23 A. Yeah. At this point, yes.

24 Q. Okay. Now, Dr. Madigan

1 calculated lifetime cumulative exposures.

2 Did you understand that?

3 A. Well, I understand it. But
4 I disagree with it.

5 Q. I understand that you
6 disagree. But do you understand that he
7 was calculating cumulative exposures?

8 A. Yes.

9 Q. Okay. Now, you didn't
10 provide any of your own calculations on
11 cumulative exposures, correct?

12 A. No.

13 Q. And you haven't done any of
14 your own calculations on cumulative
15 exposures, correct?

16 A. No.

17 Q. And you didn't provide any
18 criticisms of his calculations. You
19 provided criticisms about extrapolating
20 those calculations, but you didn't
21 provide any criticisms on the
22 calculations themselves, correct?

23 A. Well, I think that his basic
24 methods he rely to calculate exposure

1 dosing level is flawed. I don't think I
2 even needed to worry about his
3 mathematical calculation.

4 Q. Right. And when you said
5 his basic methods, you mean you have
6 concerns about him extrapolating those
7 results to NDMA and valsartan, correct?

8 A. More than that, sir. Even
9 within the dietary studies, I have a
10 great concern about his conclusion, even
11 without extrapolate the results from a
12 dietary study to valsartan.

13 Q. Okay. And that may be being
14 able to rely on the findings in the
15 dietary study itself, correct?

16 A. Correct.

17 Q. But in terms of the
18 calculations that he did, you didn't have
19 any criticisms of the calculations, just
20 how he would be able to use those
21 calculations, correct?

22 A. Well, I don't have data to
23 verify exactly the number he calculate.
24 But I understand his mathematical

1 formula. But that doesn't mean that his
2 calculated values are valid. I don't
3 know that part because I don't have the
4 data.

5 Q. Okay. I understand. You
6 didn't -- you didn't provide any
7 criticisms on the math that he did,
8 correct?

9 A. The formula he used.

10 Q. Right. You didn't provide
11 any criticisms on the math he did -- he
12 completed, or the formula that he used to
13 complete -- complete those calculations
14 of lifetime cumulative exposures,
15 correct?

16 A. See, let me answer this
17 question to you, sir. I have no problem
18 if he defines so-called a mean value of
19 this exposure time, okay, mathematically.
20 But I am not so sure that quantity can be
21 utilized to define the threshold of
22 value, beyond that value we have high
23 risk of cancer incidence. I disagree
24 with that, the application.

1 But, sir, if you ask me if
2 his mathematical formula to calculate
3 what he thinks is okay, I say, yes, his
4 mathematical formula is very simple.
5 Everybody can understand it.

6 Q. Now, you just said, "I have
7 no problem if he defines a mean value of
8 this exposure time, okay, mathematically.
9 But I am not so sure that the quantity
10 can be utilized to define the threshold
11 value, beyond that value we have high
12 risk of cancer incidence."

13 So you disagree with that
14 application.

15 Now, that opinion is nowhere
16 to be found in your report, correct?

17 A. Correct.

18 Q. And so for the first time
19 here today, you're giving that criticism,
20 correct?

21 A. Well, that's my concern. I
22 don't mean to put in the report, because
23 basically I don't even think the way he
24 derived this lifetime exposure level is

1 correct. So I don't even bother to go in
2 saying, "Your calculation is misleading,
3 even though mathematically it's correct."

4 MR. NIGH: Okay. Let's take
5 a look at LP-1558.

6 (Document marked for
7 identification as Exhibit
8 Wei-4.)

9 MR. NIGH: Let's blow up
10 that first part. This will be
11 marked as Exhibit 4, Wei
12 Exhibit 4.

13 BY MR. NIGH:

14 Q. And you see the top part
15 says, "NDMA-Contaminated Valsartan, David
16 Madigan, Ph.D." And it shows his
17 signature.

18 Do you see that?

19 A. Yes, sir.

20 Q. And this is the report that
21 you were speaking about in Number 11 in
22 terms of your report, your assignment,
23 was to review this report and provide
24 your response or criticisms of this

1 report, correct?

2 A. Yes, sir.

3 Q. Okay.

4 MR. NIGH: Let's take a look
5 at LP-1576.

6 (Document marked for
7 identification as Exhibit
8 Wei-5.)

9 BY MR. NIGH:

10 Q. And can you see that this is
11 your invoice?

12 A. Yes, sir.

13 MR. NIGH: Let's go ahead
14 and blow up that top part, the
15 very top part there, right.

16 BY MR. NIGH:

17 Q. And it starts out with
18 Bluenull LLC, and it gives an address
19 there.

20 Do you see that?

21 A. Yes, sir.

22 Q. What is Bluenull LLC?

23 A. It's a small consulting
24 group I put together more than maybe

1 15 years ago. And the basic idea is we
2 provide statistical consultations to
3 folks like this case or pharmaceutical
4 industry and government university,
5 anything related to quantitative science,
6 we provide service.

7 Q. Now, for that consulting
8 group, would you agree that the
9 pharmaceutical industry is your top
10 client?

11 A. Well, we actually had a few
12 projects with pharmaceutical industries.

13 Q. Right. Bluenull LLC has
14 received more money from pharmaceutical
15 industry than any other sector, correct?

16 A. For example, sir, as you
17 started out -- what is other sectors?

18 Q. Government, university?

19 A. Of course. Of course. We
20 don't do much for university professors.

21 Q. Okay. And so my question
22 is, you would agree that the
23 pharmaceutical industry is your top --
24 sorry. Strike that question.

1 You would agree that
2 Bluenull LLC has received more money from
3 pharmaceutical industry than any other
4 sector, correct?

5 A. Well, not quite. Depend on
6 which year. One year we work as the
7 plaintiff side for Toyota braking system,
8 security issue. The Bluenull was in the
9 plaintiffs side.

10 So we didn't work for
11 Toyota, for example.

12 So it is not really --
13 sorry, sir. It's not only --

14 Q. It's all right.

15 A. -- for pharmaceutical area.
16 Actually it's more than that. You know,
17 like, on this case, right, legal case, in
18 this sector.

19 Q. Yeah, my question isn't just
20 one year. You said that you started this
21 15 years ago. So looking over the last
22 15 years, you would agree that Bluenull
23 LLC has received more money from
24 pharmaceutical industry than any other

1 sector, correct?

2 A. Correct.

3 Q. Okay. Now, you just told me
4 about one time that Bluenull LLC
5 represented a plaintiff. And that was
6 against Toyota; is that correct?

7 A. Correct.

8 Q. And when we say Bluenull
9 LLC, were you the expert in that -- were
10 you a disclosed expert in that Toyota
11 case where you were representing the
12 plaintiff?

13 A. I was only -- I think I was
14 one of the consultant, because we have
15 many, many consultant at -- to Bluenull.
16 We probably roughly have ten professors
17 from Harvard, from Stanford, Northwestern
18 University. People actually around the
19 country actually are members of a
20 consulting group.

21 So I believe for the Toyota
22 case, we actually had more than me
23 involved in that case. That is usually
24 the case. For example, Lipitor case for

1 Pfizer, we had five -- five faculty
2 members in the group working together for
3 the case. So not only me.

4 Q. Were you personally involved
5 in the Toyota case?

6 A. Yes, sir.

7 Q. Now, other than the Toyota
8 case, were you -- did you ever represent
9 any other plaintiff?

10 A. Yes. I remember a couple
11 times we represent people accused by
12 Medicare fraud. I believe we were on the
13 plaintiff's side.

14 Q. Okay. So in a situation
15 where people are accused of Medicare
16 fraud, if you're on the plaintiff's side,
17 which party would you have been
18 representing?

19 A. We have -- represent a
20 doctor, and he was accused by Medicare,
21 and, say, overcharge patients or
22 something like that.

23 Q. So you represented the
24 doctor who is being accused of

1 overcharging patients?

2 A. Which is an inappropriate
3 accusation, in my opinion, but yes.

4 Q. I see. But in that
5 situation, you would have actually been
6 representing a defendant, correct?
7 Because he was being accused. He was the
8 accused. He was being accused of
9 overcharging patients, so he would have
10 been a defendant in that case, right?

11 A. Yes. Another case I cannot
12 release to you right now is ongoing.
13 It's from -- I also work for plaintiff,
14 because the other side is actually
15 accused.

16 I'm sorry. I get it
17 confused. It's still defendant. The
18 plaintiff's side is government.

19 Q. Okay.

20 A. The commission. But anyway,
21 I'm sorry. I apologize for that.

22 Q. So that other case that
23 you're thinking of, you actually
24 represent the defendant in that case,

1 right?

2 A. Yes. Yes.

3 Q. Okay. Other than the
4 plaintiff that you represented in the
5 Toyota case, is there any other plaintiff
6 that you've represented in your career?

7 A. For my, it's not. But I'm
8 not for sure for other consultants
9 because I don't worry about other
10 consultant in the group. Whether they
11 did, I have no idea.

12 Q. Well, for right now, my
13 questions -- take away Bluenull for now.
14 I'm just asking about you.

15 Are you aware of
16 representing, in your career, other than
17 the plaintiff in the Toyota case, any
18 other plaintiff?

19 A. No, not I can recall.

20 Q. Okay. Let's talk about the
21 Toyota case. Tell me what your
22 involvement was in the Toyota case.

23 A. Toyota case was very
24 interesting. So many years ago, people

1 bought a Toyota with electronic braking
2 system, which was new, replacing
3 so-called mechanical braking system.

4 Somehow when people step on
5 the brake, and the car, instead of
6 stopping, is accelerated. So that caused
7 some personal injury, also economic loss.

8 Economic loss was the case
9 plaintiff and -- submitted to the court.
10 And we actually helping plaintiff's side
11 to -- to actually -- against -- against
12 the Toyota. That's the case.

13 Q. And when did you get first
14 involved in that case?

15 A. When? Sir, I'm sorry?

16 Q. Approximately when did you
17 first got involved in that case?

18 A. I don't remember now. But
19 we can Google easily the case, you know,
20 using Toyota, the braking system. It
21 must pop up.

22 Q. Is it more than ten years
23 ago that you first became involved in
24 that case?

1 A. I think it's less than ten
2 years, but it's close.

3 Q. Close to ten years ago?

4 A. I cannot tell exactly.

5 Q. Okay. Yeah, I'm not asking
6 for exactly. Do you believe it was close
7 to ten years ago that you first became
8 involved in that Toyota braking case?

9 A. Sir, I really want to
10 double-check before I answer your
11 question.

12 Q. Okay. And you said that you
13 would search Google, you would see when
14 they first brought those cases, but how
15 would that tell you when you first became
16 involved? Because I don't think if we
17 search Google, it will say Dr. Wei became
18 involved -- first became involved in the
19 case at this time.

20 So how would you search
21 Google to tell when you first became
22 involved?

23 A. No, no, sir. What I'm
24 saying, you ask me when was that case. I

1 said in general we can Google to find
2 out.

3 If you're asking me
4 specifically when I was involved, I have
5 to go back to check my e-mails, if I
6 still have it, and I can get back to you
7 on that issue. I thought you were asking
8 me, when was the Toyota case, not asking
9 me when I got involved in that case.
10 Correct?

11 Q. Actually. I am asking you
12 when did you first become involved in
13 that Toyota case?

14 A. Then I cannot Google. You
15 said -- I'm not a famous person yet. So
16 I think -- but I can easily -- if I still
17 keep the e-mails, I can probably tell you
18 exactly when I was involved in Toyota
19 case.

20 Q. Would you feel comfortable
21 in saying it was between five to 10 years
22 ago?

23 A. Sir, I don't know why you
24 want me to tell you exactly the timing.

1 Is that very important to you? If it's
2 so important, I can use lunch break to
3 figure out for you.

4 Q. I'm asking you for your
5 memory. You know, I'm not asking for
6 exact times. So do you have any -- any
7 way of being able to describe about how
8 long ago that you first became involved
9 in that case?

10 A. Okay. That's fair question.
11 I don't know why it is so important for
12 this case.

13 Q. You know, let's do this. I
14 would appreciate if you don't try to
15 question why something is important. If
16 I'm asking the question, I'm allowed to
17 ask the question.

18 So let's go forward again on
19 this again.

20 Do you have any way of being
21 able to describe about how long ago that
22 you first became involved in that case?

23 A. I don't remember, sir.

24 Q. Okay. So you wouldn't be

1 able to say if it was five years ago, ten
2 years ago, or 15 years ago, as you
3 remember here?

4 A. No. Less than 15 years,
5 that's for sure.

6 Q. Less than 15. Okay. All
7 right. Back to the billing.

8 MR. NIGH: We can put that
9 back up there.

10 BY MR. NIGH:

11 Q. Okay. We can see the date
12 at the top again, if you don't mind.

13 Here we can see Bluenull,
14 and then we can see the date, August 3rd,
15 2021. And then it says, "To: Greenberg
16 Traurig," correct?

17 A. Yes.

18 Q. And it's your understanding
19 that it was Greenberg Traurig who
20 retained you for this case?

21 A. I'm sorry, sir. Say it
22 again, please.

23 Q. Were you retained on behalf
24 of Greenberg -- on behalf of Teva or by

1 Greenberg Traurig?

2 A. Yes, sir.

3 Q. Okay. And taking a look
4 down, we can see your hours. And it says
5 that you spent a total of 45.65 hours on
6 this project between July 9th and
7 August 2nd.

8 Do you see that?

9 A. Yes, sir.

10 Q. Now, that would be, you
11 know, over 45 hours in less than a month,
12 correct?

13 A. Yes, sir.

14 Q. And you only first became
15 involved July 9th after Dr. Madigan
16 submitted his expert report on July 6th,
17 correct?

18 A. I don't remember on July 9th
19 I got exactly Dr. Madigan's report that
20 day or not. But I remember I got a
21 listing of references from the lawyers on
22 July 9th asking me to review.

23 Q. Okay. So Dr. Madigan
24 submitted his report at the beginning of

1 July.

2 MR. NIGH: Actually, let's
3 go back to Madigan's report.
4 LP-1558.

5 Let's blow up the signature
6 and the date.

7 BY MR. NIGH:

8 Q. Do you see that signature,
9 and, right below it, it's signed July 7,
10 2021?

11 A. Yes, sir.

12 Q. So you only -- you only
13 became involved a couple days after the
14 date of this expert report, correct?

15 A. Correct.

16 Q. Okay. Let's go back to your
17 billing. And when you first were
18 involved, my understanding is on
19 July 9th, you got a list of references
20 from the defense attorneys, correct?

21 A. Correct.

22 Q. And then you also had a
23 DropBox with those studies, correct?

24 A. I don't think on July 9th I

1 got a listing from the DropBox yet.

2 Q. Okay. Do you know
3 approximately when you got the DropBox of
4 studies?

5 A. I'm not quite sure. Maybe a
6 week afterward, like three or four days.
7 I don't recall, sir.

8 Q. Okay. If we take a look at
9 the bottom here, the next page. It shows
10 August 2nd, .8 hours.

11 Do you see that?

12 A. Yes, sir.

13 Q. Now -- and that's the last
14 date on this invoice.

15 Between August 3rd and
16 today, how long -- how many more hours
17 have you spent on this case?

18 A. I don't know exactly the
19 number of hours, sir. I need to go back
20 and check my e-mails. I haven't
21 tabulated the number of hours that I've
22 been working on this case after
23 August 3rd.

24 Q. Okay. Do you see how each

1 of these dates has a number of hours,
2 7/23, three hours; 7/24, 6 hours; 7/25,
3 2.5 hours?

4 Would you be writing down
5 those hours simultaneously as doing the
6 work each day?

7 A. No. What happens in my
8 practice -- I don't know other
9 consultants. At end of the day, I
10 just -- every time I had a conference
11 call, I roughly estimate how many minutes
12 I been on the call that day.

13 Usually I write it up right
14 away after the call and how many hours I
15 reviewed the documents right after I'm
16 recording how many hours, piece by piece.
17 Then end of the day, I actually put up a
18 number, add the total number of hours for
19 that day.

20 Q. Okay. And so at the end of
21 the day you would total up your number of
22 hours for each day that you spent time on
23 this case, correct?

24 A. Yes, sir.

1 Q. Did you keep doing that
2 after August 3rd?

3 A. I believe so, yes.

4 Q. So where do you keep that
5 information, the number of hours that you
6 spent each day?

7 A. I'm not very good at
8 lawyers. I know my assigned lawyer, he
9 has very good software to doing this kind
10 of thing.

11 I usually just very casually
12 put in an e-mail, and I put it -- e-mail,
13 send it to myself, so I have a record.
14 And then towards the end of the day, I
15 just go through this and add it up.

16 Q. So that's what I'm asking
17 for. I'm not asking for each individual,
18 you know, e-mail. I'm asking for where
19 do you tabulate at the end of the day,
20 where do you keep those hours? You say
21 at the end of the day you add them up.
22 You put them somewhere. Where do you put
23 those hours that you've added up at the
24 end of each day?

1 A. Basically, for example, I
2 have three e-mails related to the case
3 today. And end of the day, I look at
4 three, the last e-mail, I just put it
5 down the total number for that date,
6 that's it.

7 Q. Oh, I see. So what you're
8 doing is your last piece of work
9 assignment or last e-mail that you
10 received for the day, you will put your
11 total number of hours in that e-mail?

12 A. Yes, sir.

13 Q. Okay. So you would need to
14 go back through each of those e-mails to
15 be able to get the total number of hours
16 that you've completed since August 3rd,
17 correct?

18 A. Yeah, very inefficient, but
19 that's the way I did it for many years.

20 Q. Okay. What's your best
21 estimate in terms of your total number of
22 hours that you spent between August 3rd
23 and today?

24 A. My best estimate, probably

1 30 or 35 hours total. But I'm not quite
2 sure. I haven't counted today's yet. I
3 don't know how many hours that you're
4 going to spend with me or even tomorrow.

5 Q. No, I understand. I'm
6 talking about -- let's -- your best
7 estimate before -- let's say between
8 August 3rd and yesterday, is it still 30
9 to 35 hours?

10 A. Yeah. Sorry.

11 Yeah, I think it's between
12 30 and 35. That's my rough guess, sir.
13 Again, I apologize, I don't know exactly
14 the number.

15 Q. Okay. Do you believe the
16 valsartan -- the NDMA in dietary studies
17 or the NDMA is somehow different --
18 sorry. Strike that.

19 Do you believe the NDMA --
20 exogenous NDMA in foods is somehow
21 different or acts differently than the
22 NDMA in valsartan?

23 A. Sir, I am not a
24 toxicologist. I cannot make that

1 comment. I have no opinion on this.

2 Q. Okay. And you're not a
3 pharmacologist either, so you haven't
4 looked at anything in regards to
5 pharmacokinetics, correct?

6 A. Correct.

7 Q. Okay.

8 MR. NIGH: Let's take a look
9 at LP-1474.

10 (Document marked for
11 identification as Exhibit
12 Wei-6.)

13 MR. NIGH: This will be
14 marked as Exhibit -- Wei
15 Exhibit 6.

16 BY MR. NIGH:

17 Q. At the bottom, you can see
18 World Health Organization, Geneva 2002.

19 And in the center you can
20 see nitrosodimethylamine.

21 Do you see that?

22 A. Yes, sir.

23 Q. Do you know what
24 nitrosodimethylamine stands for -- or

1 what that is?

2 A. I thought that is the DM --
3 NDMA; is that correct?

4 Q. Yes. And so this is a
5 report from the WHO in 2002 on NDMA.

6 Before today, have you ever
7 seen this?

8 A. I did see it. I didn't read
9 it word by word. And I did a glance
10 over.

11 Q. Okay. So you have seen this
12 before today?

13 A. Yes.

14 Q. And you said that you
15 glanced over it?

16 A. Yes.

17 Q. Okay. Let's take a look at
18 Page 4.

19 MR. NIGH: Let's blow up the
20 paragraph on the right side, third
21 paragraph down.

22 BY MR. NIGH:

23 Q. And here it says, "Based
24 upon laboratory studies in which tumors

1 have been induced in all species,
2 examined at relatively low levels, NDMA
3 is clearly carcinogenic."

4 Do you see that?

5 A. Yes, sir.

6 Q. Now, today, you're not
7 offering any opinions as to whether or
8 not NDMA is carcinogenic, correct?

9 A. No.

10 Q. Okay. And also you didn't
11 review any of the laboratory studies in
12 which tumors were being induced in
13 species when administered NDMA, correct?

14 A. Correct.

15 Q. Okay. Here, next it says,
16 "There is overwhelming evidence that NDMA
17 is mutagenic and clastogenic."

18 Do you know what mutagenic
19 and clastogenic refer to?

20 A. No, sir.

21 Q. Okay. At the bottom it
22 shows, "Qualitatively, the metabolism of
23 NDMA appears to be similar in humans and
24 animals. As a result, it is considered

1 highly likely that NDMA is carcinogenic
2 to humans, potentially at relatively low
3 levels of exposure."

4 Do you see that?

5 A. Yes, sir.

6 Q. And you did not review human
7 tissue studies where they were analyzing
8 the metabolism of NDMA, correct?

9 A. Right.

10 Q. Taking a look at the next
11 page, on the upper left corner.

12 It says, "Cancer is clearly
13 the critical endpoint for quantification
14 of exposure relationship for risk
15 characterization of NDMA. In addition to
16 it being best characterized, in general,
17 tumors occur at lowest concentration
18 compared with those typically reported to
19 induce noncancer effects."

20 Do you see that?

21 A. Yes, sir.

22 Q. And you didn't perform any
23 sort of risk assessment analysis in terms
24 of looking at, you know, at what levels

1 or concentrations of NDMA tumors would be
2 induced, either in animals or humans,
3 correct?

4 A. No, sir. But that was not
5 on my assignment.

6 Q. Okay. And then at the
7 bottom it says, "NDMA is a genotoxic
8 carcinogen and exposure should be reduced
9 to the extent possible."

10 Do you see that?

11 A. Yes, sir.

12 Q. And you have no reason to
13 disagree with the WHO when they say that
14 NDMA is a genotoxic carcinogen and
15 exposure should be reduced to the extent
16 possible, correct?

17 A. Well, it depend on disagree,
18 or agree. You asking me. I said this
19 document is very old, almost 20 years
20 old. I'm surprised they didn't even
21 up-to-date this website or the report.
22 I'm surprised this is 20 years old, the
23 document is still existing.

24 Q. I'm sorry. You're surprised

1 they haven't updated this report since
2 then?

3 A. You know it's 20 -- almost
4 20 years, right, sir.

5 Q. Have you seen updated
6 reports from various --

7 A. No.

8 Q. -- agencies where they
9 updated their analysis on NDMA?

10 A. I don't think they have
11 updated, as far as I know.

12 Q. As far as you know, you are
13 not aware of any other agencies, health
14 agencies or regulatory agencies that have
15 updated their opinions on NDMA and
16 whether or not it's reasonably
17 anticipated to be carcinogenic?

18 A. I don't think -- if there is
19 one, I would be happy to read it, sir.

20 MR. NIGH: Let's take a look
21 at 23.

22 BY MR. NIGH:

23 Q. Now, other than the update,
24 the question on whether or not it's been

1 updated in 20 years, do you have any
2 other reasons to disagree?

3 A. Well, I'm not a -- I'm
4 sorry, sir. I don't mean to talk over
5 you. I'm sorry. Why don't you finish.

6 Q. No, that's okay. Do you
7 have any other reasons to disagree with
8 the WHO?

9 A. No, sir. I don't know this
10 WHO's position, you call this document,
11 or paper, whatever you want, right. But
12 I'm saying in general, any animal study
13 trying transported to human study, and we
14 know very well, sometimes just doesn't
15 work. It's trivial.

16 And that's why we need human
17 studies to confirm what the WHO, the
18 position papers, right. But I'm
19 surprised, so many papers published
20 afterwards, WHO did not have updated
21 version. That's my understanding, right.
22 If you have updated version, I'd be happy
23 to read it.

24 Q. But my understanding is that

1 you haven't reviewed any updated position
2 papers from any of the agencies that
3 have, you know, discussed NDMA and it
4 being a probable carcinogen and/or
5 reasonably anticipated to be a human
6 carcinogen, correct?

7 A. Yeah, from human being --
8 from human being studies.

9 Q. Okay. Let's take a look
10 at -- now, if there were other regulatory
11 agencies that have looked at updated
12 epidemiological studies and included that
13 in their assessment, isn't that something
14 that you would want to review?

15 A. Oh, yeah, for sure. I'd
16 love to read it.

17 MR. NIGH: Okay. Let's take
18 a look at 23 on the right side.

19 First paragraph.

20 BY MR. NIGH:

21 Q. And here they say, WHO says,
22 "Therefore, owing to the considerable
23 evidence of carcinogenicity of NDMA in
24 laboratory species, evidence of direct

1 interaction with DNA consistent with
2 tumor formation, and the apparent lack of
3 qualitative species-specific differences
4 in the metabolism of this substance, NDMA
5 is highly likely to be carcinogenic to
6 humans."

7 Do you see that?

8 A. Yes, sir.

9 Q. Now, I just want to confirm,
10 you didn't look at any studies on NDMA in
11 laboratory species, correct?

12 A. Correct.

13 Q. You didn't look at any
14 studies on the evidence of direct
15 interaction with DNA consistent with
16 tumor formation, correct?

17 A. Correct.

18 Q. And you didn't look at any
19 studies that showed whether or not there
20 was an apparent lack of qualitative
21 species-specific differences in the
22 metabolism of NDMA, correct?

23 A. Correct.

24 MR. NIGH: Okay. We can put

1 this away.

2 BY MR. NIGH:

3 Q. We've been going over a
4 little over an hour. Would you like to
5 take a break about now?

6 A. No. If you want to take a
7 break, you know, go ahead. But I'm okay.

8 Q. Okay. Let's keep going.

9 All right. We'll take a
10 look at LP-1577. This is your report
11 again.

12 Now, Doctor, during
13 Dr. Panigrahy's deposition, defense
14 counsel asked Dr. Panigrahy multiple
15 questions regarding a couple of sentences
16 that he had that were identical between
17 his Actos report and his valsartan
18 report, a couple sentences out of a
19 256 -- 250-plus-page report that he
20 submitted in valsartan.

21 Did you review that
22 testimony at all?

23 A. No, I don't.

24 Q. Now, would you be worried

1 yourself about a criticism like that,
2 that there are identical sentences from
3 one past expert report versus a -- the
4 report that you produced here today?

5 MR. MERRELL: Objection to
6 form.

7 THE WITNESS: I'm not quite
8 sure of your question. You said
9 am I worried about it? I didn't
10 have access to other experts'
11 reports? Is that what your
12 question?

13 BY MR. NIGH:

14 Q. Would you personal --

15 A. I don't understand your --

16 Q. Would you be personally
17 worried if there was a problem with
18 cutting and pasting or having identical
19 sentences from a past expert report and
20 the expert report you've submitted in
21 valsartan?

22 MR. MERRELL: Objection to
23 form.

24 THE WITNESS: I'm not quite

1 sure which part you're talking
2 about. For example, for my
3 quantification, usually I usually
4 use older things. I use it many,
5 many times for legal case, almost
6 identical, except for up-to-dated
7 the number of publications or new
8 award I received.

9 I just simply up-to-date it.
10 If you said, well, you know, you
11 shouldn't cut and paste from
12 previous report. I say, well,
13 it's my report. I can do anything
14 that I wanted to, right. I can
15 copy every word I wanted to, as
16 long as it reflect the truth.

17 BY MR. NIGH:

18 Q. So it's your belief that --
19 you know, not just qualifications, but if
20 you had it in a prior report, that you
21 could do anything you wanted with that
22 prior report and cut and paste or copy
23 any word that you wanted from a prior
24 report into this report, as long as it

1 reflects the truth, correct?

2 A. Well, you say any word.

3 That's a very strong word, sir. I

4 just -- we can repeat many, many word,

5 right. I mean, I don't mean to play the

6 word game here with you, sir. I'm just

7 wondering what is wrong with me citing

8 the principle of statistical methods,

9 right? That's the same old thing, right?

10 Why should I every time write a legal

11 expert witness report, I have to redo it

12 changing the wording with the time,

13 because the principle is there.

14 The same wording, we can use

15 repeatedly. Then for this case, what's

16 new? Then I'm going to add in my new

17 opinions, right? I don't see anything

18 wrong with that, sir.

19 Q. So it's your testimony that

20 if it's the same principle that's being

21 repeated from a past report into this new

22 report, that you don't have any problem

23 with it having the exact words, as long

24 as it's the same principle that's being

1 applied for both reports, correct?

2 A. Correct.

3 Q. Fair enough. Okay.

4 MR. NIGH: Let's take a look
5 at -- let's take a look at
6 LP-1562.

7 (Document marked for
8 identification as Exhibit
9 Wei-7.)

10 MR. NIGH: Let's go ahead
11 and blow up the In Re Bextra and
12 Celebrex Marketing.

13 BY MR. NIGH:

14 Q. Do you see this, Doctor?

15 A. Yes.

16 Q. It says expert report of
17 Professor -- and it's you, right,
18 Dr. Wei?

19 A. Yes, sir.

20 Q. Okay. And here it says,
21 "Name of expert, Dr. Wei." And it says,
22 "Representing the defendant."

23 Is that accurate, that in
24 the Celebrex case, you were representing

1 the pharmaceutical industry defendant?

2 A. Yes, sir.

3 Q. Okay. And let's take a look
4 below.

5 MR. NIGH: If we can blow up
6 the table of contents.

7 BY MR. NIGH:

8 Q. Here, you had a table of
9 contents for this report.

10 Do you see that?

11 A. Yes, sir.

12 Q. And then we can take a look
13 at the next page.

14 MR. NIGH: Let's blow up the
15 table of contents there as well.

16 BY MR. NIGH:

17 Q. And that continues with the
18 table of contents that you have with this
19 report.

20 Do you see that?

21 A. Yeah.

22 Q. And then let's look at
23 introduction.

24 And it says, "1. I received

1 a Ph.D. degree in statistics in 1975 from
2 the University of Wisconsin. I have been
3 a tenured professor of biostatistics at
4 Harvard University since 1991 and a
5 professor of biostatistical science and
6 computational biology at Dana Farber
7 Cancer Institute, Harvard Medical School,
8 since 1997."

9 Do you see that?

10 A. Yes, sir.

11 Q. This is describing you,
12 correct?

13 A. Sorry, sir. Say again.

14 Q. I said this is -- these
15 qualifications are describing you,
16 correct?

17 A. Yes, sir.

18 Q. Okay. And looking at
19 assignment, Number 4. Assignment, it
20 says, "I have been asked to determine
21 whether Celebrex, at a daily dose of
22 200 milligrams, 400 milligrams, and
23 800 milligrams is associated with the
24 specific risk of cardiovascular events

1 relative to placebo and non-selective
2 nonsteroidal antiinflammatory drugs based
3 on reliable datasets accessible to me
4 from comparative clinical trials."

5 Do you see that?

6 A. Yes, sir.

7 Q. And so in the Celebrex case
8 you had clinical trials that you were
9 analyzing, correct?

10 A. Yes, sir.

11 Q. Are you aware of any
12 clinical trials in this case that have
13 compared people contaminated with NDMA,
14 valsartan -- or people taking
15 contaminated NDMA valsartan compared to
16 people taking uncontaminated valsartan?

17 A. No, sir.

18 Q. There aren't any such
19 clinical trials that would be of
20 relevance in terms of your opinion for
21 this question that you've looked at in
22 valsartan, correct?

23 A. I don't have it actually.
24 The only thing that I'm worried about

1 is -- or concerned about is Dr. Madigan's
2 references.

3 Q. Right. And so in the
4 valsartan -- in the valsartan case, you
5 actually haven't looked at any data
6 regarding clinical trials, correct?

7 A. No, sir.

8 Q. Let's put that one to the
9 side. We'll come back to it later.

10 MR. NIGH: Let's take a look
11 at LP-1561.

12 (Document marked for
13 identification as Exhibit
14 Wei-8.)

15 MR. NIGH: This will be
16 marked as Wei Exhibit 8.

17 BY MR. NIGH:

18 Q. Here you see it says, "In Re
19 Taxotere Products Liability Litigation."

20 The date shows February 8,
21 2019.

22 Do you see that?

23 A. Yes, sir.

24 Q. Do you recall just giving

1 your Taxotere expert report a little over
2 two years ago?

3 A. I vaguely remember, but not
4 very detailed anymore.

5 Q. Okay. And here it says,
6 "Expert report of Dr. Wei," correct?

7 A. Yes, sir.

8 Q. Okay. And again, you were
9 representing the defendant pharmaceutical
10 company in this case, correct?

11 A. Correct.

12 Q. And in the introduction --
13 if you see the introduction, which is the
14 first couple sentences, it says, "I
15 received a Ph.D. in statistics from the
16 University of Wisconsin. I have been a
17 tenured professor of biostatistics at
18 Harvard University since 1991 and was a
19 professor of biostatistical science and
20 computational biology at Dana Farber
21 Cancer Institute, Harvard Medical School,
22 between 1997 and 2012."

23 Correct?

24 A. Yes, sir.

1 Q. So this again, this is
2 describing you, correct?

3 A. Yes, sir.

4 MR. NIGH: Let's take a look
5 at LP-1579.

6 (Document marked for
7 identification as Exhibit
8 Wei-9.)

9 MR. NIGH: This is being
10 marked as Exhibit 9.

11 BY MR. NIGH:

12 Q. Here it says, "Bone Care
13 International LLC and Genzyme
14 Corporation."

15 Do you see that?

16 A. Yes, sir.

17 Q. And here it says, Doctor --
18 it's an expert report on October 30,
19 2009, correct?

20 A. Yes, sir.

21 Q. And Bone Care International
22 LLC, that's another -- that's a
23 corporation. The plaintiff here is a
24 corporation, correct?

1 A. Sorry, back in 2009, my
2 memory is really fuzzy about this case.
3 So if you can remind me of what's going
4 on, I would really appreciate it.

5 Q. Okay. Let's take a look at
6 the -- let's take a look under summary of
7 opinion.

8 It says, "I have been asked
9 by counsel for Genzyme to investigate
10 whether there is a difference in
11 treatment of secondary hyperthyroidism
12 in" -- "hyperparathyroidism in patients
13 with end stage renal disease using
14 either" -- I'm not sure I can pronounce
15 that. -- "doxercalciferol administered
16 intravenously or calcitriol administered
17 intravenously with respect to side
18 effects using data from two studies that
19 were reported."and then it gives those
20 cites.

21 Do you see that?

22 A. Yes, sir.

23 Q. Does that help refresh your
24 recollection?

1 A. No, not really. It has been
2 too long.

3 Q. Do you know that in this
4 case you were representing a corporation?

5 A. Say it again, sir.

6 Q. Do you know that in this
7 case you were representing a corporation?

8 A. I'm not quite sure I
9 understand your question. I mean, I'm
10 representing Genzyme here, right.

11 Q. Genzyme.

12 A. Right.

13 Q. Do you know that Genzyme is
14 a corporation?

15 A. Yeah, it used to be by
16 itself, an independent drug company.
17 They bought by Sanofi, I think.

18 Q. I see. So Genzyme is a
19 pharmaceutical industry corporation,
20 correct?

21 A. Yes, sir.

22 Q. Got it. So this is another
23 case where you're representing
24 pharmaceutical industry, correct?

1 A. Well, sir, if I remember,
2 the plaintiff was also a corporation.

3 Q. Right.

4 A. It's not like -- it is fair
5 game.

6 Q. It's pharmaceutical company
7 against pharmaceutical company, and you
8 were representing one of the
9 pharmaceutical companies, correct?

10 A. Yes, sir.

11 MR. NIGH: Okay. Let's go
12 up on this expert report at the
13 top of the page, and it says --
14 where -- three and four, let's
15 highlight that all the way down to
16 summary of opinions, yes.

17 BY MR. NIGH:

18 Q. Here it says, my CV -- I'm
19 not going to go into that.

20 Number 4, it says, "My
21 previous deposition and trial experience
22 is as follows."

23 And it shows Western
24 Division Cincinnati Services.

1 Do you see that?

2 A. Yes.

3 Q. And you represented the
4 defendant in that case, correct? Do you
5 see where it says defendant?

6 A. Sorry, yeah. I -- for the
7 defendant, yes, sir.

8 Q. And next is Ortho Biotech
9 Products versus Amgen.

10 Do you see that?

11 A. Yes, sir.

12 Q. And you represented the
13 plaintiff, but here the plaintiff is a
14 pharmaceutical industry, correct?

15 A. Yeah. This is a corporation
16 against a corporation, yes.

17 Q. Pharmacy industry against
18 pharmacy industry again, correct?

19 A. Correct.

20 Q. And next it says, Bracco
21 Diagnostics versus Amersham Health
22 Incorporated.

23 Do you see that?

24 A. Correct.

1 Q. And here it says for
2 defendant and plaintiff. Did you
3 represent both the defendants and the
4 plaintiffs in this case?

5 A. Well, this is interesting
6 case. Actually, they're suing each
7 other.

8 So in one case -- it's the
9 same company.

10 Q. Right. But this is
11 another -- this is another one of, you
12 know, pharmaceutical industry against
13 pharmaceutical industry, correct?

14 A. Correct.

15 Q. Okay. And so you would have
16 represented pharmaceutical industry in
17 that case, correct?

18 A. Against another one, yes.

19 Q. And then next we have
20 Howmedica Osteonics versus Zimmer.

21 Do you see that?

22 A. Yes.

23 Q. And you represented Zimmer
24 here, correct?

1 A. I apologize. I don't
2 remember now. This is 2007.

3 Q. It says, for defendant.
4 Do you see that?

5 A. Yeah, I mean, again, if it's
6 against Zimmer, then I'm for the
7 defendant, yes.

8 Q. But nonetheless, here again,
9 I know we keep saying pharmaceutical.
10 But medical device and pharmaceutical
11 company. This is another one of those
12 where we see pharmaceutical/medical
13 device company against
14 pharmaceutical/medical device company,
15 correct?

16 A. Correct.

17 Q. Okay. And so you've
18 represented again a pharmaceutical
19 company/medical device company, correct?

20 A. Correct.

21 Q. And then we saw Bextra and
22 Celebrex. And you represented a
23 pharmaceutical company in that case,
24 correct?

1 A. Yes, sir.

2 Q. And then In Re Pfizer, is
3 the next one, securities litigation. And
4 you represented the pharmaceutical
5 company in that case as well, correct?

6 A. Yes, sir.

7 Q. Okay. Is it fair to say
8 that the vast majority of your expert
9 opinions are on behalf of pharmaceutical
10 companies?

11 A. Yeah, as you can see,
12 against another company, not really
13 against an individual cases.

14 Q. Right. But my question is
15 not necessarily who they are against.
16 But the vast majority of your
17 representation would be on behalf of
18 pharmaceutical companies or medical
19 device companies, correct?

20 A. Yeah, for some -- you know,
21 I'm really impressed, sir, you dig out of
22 the interesting case that I was working.

23 The second -- the first one,
24 Western Division Cincinnati Women, that

1 was a really interesting abortion case.
2 And I was not concerning about any
3 company or anything. It's actually we
4 fight for women's right.

5 The other side -- you know,
6 that's a very interesting case, actually.

7 Q. Well, interesting that you
8 brought that up. But you about you were
9 actually on the side of the defendant,
10 where you were looking to uphold a law
11 that actually made it more difficult for
12 women to be able to have abortions after
13 a certain time frame, correct?

14 A. Correct, yes.

15 Q. Okay. So you weren't
16 actually in that case fighting on behalf
17 of women's rights. You were actually on
18 the other side, right?

19 A. Yeah, you're right.

20 Q. Okay. Other than that case,
21 wouldn't you agree with me that the vast
22 majority of your opinions are on behalf
23 of pharmaceutical companies or on behalf
24 of medical device companies?

1 A. Yes, sir.

2 MR. NIGH: Okay. Let's go
3 ahead and take a look at LP-1577.
4 We'll mark this as Wei Exhibit 10.

5 (Document marked for
6 identification as Exhibit
7 Wei-10.)

8 BY MR. NIGH:

9 Q. Here you can see it's called
10 A Woman's Choice East Side Women's Clinic
11 versus Scott Newman.

12 Do you see that? It says,
13 et cetera, et al., defendants?

14 A. Yep.

15 Q. And this is the case that we
16 were just talking about, right?

17 A. Yeah.

18 Q. Okay. And this is the case
19 where you were on the side of trying to
20 uphold the law that made it more
21 difficult for women to get abortions,
22 correct?

23 A. Sir, I'm not so for sure
24 that I would use your word "more

1 difficult" for women seeking abortion. I
2 think that's not appropriate word.

3 We are asking the court
4 upheld the law established by the state
5 of Indiana, Ohio, was --

6 Q. Well, this is a law. Sorry.
7 I didn't mean to interrupt you. Go
8 ahead.

9 A. So if I remember, sir, this
10 is a 1999, right?

11 Q. Yeah.

12 A. That was a long, long time
13 ago. And if I remember correctly, the
14 Indiana, example, state, had some kind of
15 abortion rules, right. For example, in
16 Mississippi, I believe it's like 24 hours
17 or 48 hours waiting period. Forgive me,
18 sir. I don't remember detail anymore.

19 Basically, just saying,
20 look, if a woman looking for abortion
21 after first contact with the clinic, and
22 she should wait about a time -- I don't
23 know one day or two days. Then go
24 backwards.

1 Some people were just
2 wondering, maybe they can settle down and
3 reconsider the situation after they got
4 the information from the clinic and they
5 can actually make a better decision
6 instead of, like, walking into the
7 clinic, like I go to fast food store or
8 like a McDonalds, right?

9 If I want to have abortion,
10 then I'm going to do right away. So
11 that's basically the principle, should we
12 have this waiting period.

13 And the state legislature
14 established and say could you please keep
15 this rule.

16 That's what my
17 understanding, my memory, my
18 recollection.

19 Q. Do you recall stating in
20 here that you would agree with a law that
21 says banning abortions after 15 weeks of
22 pregnancy that you would support that?

23 A. I don't remember exactly the
24 weeks of the pregnancy anymore, sir.

1 This has been long time.

2 Q. Okay.

3 MR. NIGH: Let's move on
4 from that. Let's go ahead and
5 take a break at this point.

6 THE VIDEOGRAPHER: The time
7 right now is 10:34 a.m. We're off
8 the record.

9 (Short break.)

10 THE VIDEOGRAPHER: The time
11 right now is 10:54 a.m. We're
12 back on the record.

13 BY MR. NIGH:

14 Q. Now, doctor, remember we
15 were talking about cutting and pasting
16 from prior reports. And you said that it
17 wouldn't be uncommon for you to cut and
18 paste information from your
19 qualifications into your reports,
20 correct?

21 A. Sorry, Counsel, your picture
22 is so fuzzy.

23 Okay. What I was saying,
24 sir, is this, like, my job description, I

1 think it's perfectly all right to just
2 use the same old language, right.
3 Nothing wrong with that.

4 If I stated the principle,
5 the principle of a statistical method,
6 that never changes so far, it is all
7 right.

8 But if you're actually
9 dealing with a new case, if a new
10 situation, then I don't think we just
11 repeat what we said before, right, which
12 may not be relevant.

13 Q. I'm not going to look at
14 your qualifications for now in terms of
15 comparing your results. I'm going to
16 look at your analysis. Okay. We're
17 going to skip past qualifications.

18 I think you would agree with
19 me that you would commonly take the same
20 information in your qualifications in one
21 report and put it into other reports,
22 correct?

23 A. Correct. Sorry, Counsel.
24 Could you show your picture again? Could

1 talk again. I think I want to click
2 again. It's very fuzzy somehow.

3 MR. MERRELL: It's fuzzy for
4 me too.

5 MR. NIGH: Okay. Let's go
6 ahead and get off the record and
7 see if we can fix the fuzziness.

8 THE VIDEOGRAPHER: The time
9 right now is 10:56 a.m. We're off
10 the record.

11 (Brief pause.)

12 THE VIDEOGRAPHER: The time
13 right now is 10:58 a.m. We're
14 back on the record.

15 BY MR. NIGH:

16 Q. Okay. I think you would
17 agree with me that you would commonly
18 take the same information in your
19 qualifications in one report and put it
20 into other expert reports, correct?

21 A. Correct.

22 Q. Okay. Let's -- what I want
23 to do is get past that and look at your
24 analyses between -- and compare it

1 between these reports.

2 MR. NIGH: So let's go ahead
3 and, side by side, I want to have
4 LP-1557 and LP-1561.

5 BY MR. NIGH:

6 Q. Side by side, we're going to
7 look at your expert report that you
8 provided here in valsartan with your
9 expert report that you provided in
10 Taxotere. Okay.

11 MR. NIGH: Let's take a look
12 at Page 7 of the valsartan report.
13 Valsartan, go to Page 7. Yes.
14 And then on Taxotere we will go to
15 Page 2.

16 Let's blow up this first
17 paragraph for valsartan that
18 starts with "Suppose." Let's blow
19 that up.

20 And then let's blow up on
21 the other side Paragraph 12 that
22 starts with "Suppose."

23 And let's -- can we make
24 that just a tad bit, I'm not sure

1 if it's to make that other
2 "suppose" bigger.

3 BY MR. NIGH:

4 Q. What we see, on the left
5 side is your expert report, valsartan.
6 It starts off with, "Suppose that we are
7 interested in the rate of occurrence of a
8 certain clinical event, for example,
9 cancer, among subjects exposed to NDMA or
10 NDEA and their counterparts are control."

11 On the Taxotere side, it
12 says, "Suppose that we are interested in
13 the rate of occurrence of a certain
14 clinical event, for example, permanent
15 alopecia among patients treated with
16 Taxotere relative to its counterpart,
17 control, for patients who have been
18 exposed to other treatments."

19 Do you see that?

20 A. Yes, sir.

21 Q. Now, you would agree that
22 the structure of those sentences are very
23 similar, and essentially what it appears
24 you have done is take out what was

1 relevant to Taxotere and plug in what's
2 relevant for valsartan, correct?

3 A. Well, that's -- I change the
4 word here, right. Not exactly copied the
5 same old thing like on the left --
6 right-hand side.

7 Q. Right. At the time that
8 you're doing your valsartan report, you
9 had your Taxotere report. And you used
10 the Taxotere report as your framework for
11 the valsartan report, correct?

12 A. For statistical principles
13 here.

14 Q. Right. But you used your
15 Taxotere report as your framework for
16 your valsartan report, correct?

17 A. I used the same -- similar
18 format to describe statistical
19 methodologies from Taxotere case to the
20 valsartan case.

21 Q. Okay. And in fact, you used
22 a lot of similar word structure
23 throughout the report in Taxotere
24 compared to your report in valsartan,

1 correct?

2 A. For statistical principle,
3 yes.

4 Q. Well, let's look at the next
5 line. It says -- in the next line, it
6 says, "In the first step" -- on the
7 valsartan side. "In the first step, and
8 we take a sample from a population of
9 subjects exposed and another example from
10 the population of subjects who were not
11 exposed."

12 On the Taxotere side, "In
13 the first step, we take a sample of the
14 population of patients treated with
15 Taxotere and another example from the
16 population of patients who did not
17 receive Taxotere."

18 You would agree those
19 sentences are very similar, correct?

20 A. Correct.

21 Q. On the left -- on the left
22 side, your valsartan report, you say,
23 "Assuming that these samples are valid
24 representatives of the two populations,

1 quantitative analytic methods can be used
2 to determine whether the exposed group
3 has higher, lower, or similar event rate
4 than that for the control group."

5 On the other side, you say,
6 "Assuming" -- on Taxotere, you say,
7 "Assuming that the samples are valid
8 representatives of two populations,
9 quantitative analytic methods can be used
10 to determine whether the Taxotere group
11 has a higher, lower, or similar rate" --
12 "event rate than that for the
13 non-Taxotere group."

14 Do you see that?

15 A. Yes, sir.

16 Q. You would agree those
17 sentences are very similar, correct?

18 A. Yes, sir.

19 Q. Next, on the valsartan side,
20 it says, "Since we draw conclusions based
21 on a subset of subjects, any qualitative
22 or quantitative interpretation of the
23 result, whether the rate is higher or
24 not, is subject to sampling error."

1 On the Taxotere side, you
2 say, "Since we draw conclusions based on
3 a subset of patients, any qualitative or
4 quantitative interpretation of the
5 result, whether the rate is higher or not
6 is subject to sampling error."

7 Correct?

8 A. Yep.

9 Q. Those are sentences that
10 appear in both these reports, correct?

11 A. Correct.

12 Q. On the valsartan side, you
13 say, "That is, the observed event rate
14 may be higher leading to a possible false
15 positive finding."

16 MR. NIGH: And we can go
17 down to the next -- yep, very
18 good. There.

19 BY MR. NIGH:

20 Q. "That is, the observed event
21 rate may be higher, leading to a possible
22 false positive, or lower leading to a
23 possible false negative finding, than the
24 true event rate in the population."

1 On the other side you have,
2 "That is" -- for Taxotere, you have,
3 "That is, the observed event rate may be
4 higher, leading to a possible false
5 positive finding or lower leading to a
6 possible false negative finding than the
7 event rate in the population."

8 Those are the exact
9 sentences, correct, in both reports?

10 A. Yes, sir.

11 Q. Next, going down on the
12 valsartan side, on Page 8, it shows, "An
13 efficient statistical method for
14 analyzing such data minimizes the chance
15 of making these two types of errors."

16 And then on the Taxotere
17 side, it says, "An efficient statistical
18 method for analyzing such data minimizes
19 the chance of making these two types of
20 errors."

21 Those are exact sentences in
22 each of those reports, correct? Correct?

23 A. Yes, sir.

24 Q. On the left side it says,

1 "It is important to note that except for
2 the exposure to NDMA or NDEA, the exposed
3 subjects in the sample should be similar
4 to the subjects in the non-exposed sample
5 with respect to important observable or
6 unobservable confounders."

7 On the right side you say,
8 "It is important to note that except for
9 treatment with Taxotere, Taxotere users
10 in the sample ideally should be similar
11 to patients in the non-Taxotere sample
12 with respect to important observable or
13 unobservable confounders." And then you
14 list, "E.g., age, disease status, et al."

15 Do you see that?

16 A. Yes, sir.

17 Q. Those sentence -- that part
18 of the sentence is very, very similar in
19 both of the reports, correct?

20 A. Well, I missed example age
21 and disease status.

22 Q. Right. You didn't list any
23 examples in valsartan. You just listed
24 them in Taxotere, correct?

1 A. Yeah. Well, it's not
2 identical. But I missed that part.

3 Q. Okay. Let's take a look at
4 18 on valsartan. And let's scroll down
5 to the next paragraph.

6 So you followed that
7 principle in your report in Taxotere with
8 the same principle that you followed in
9 your report with valsartan, Number 18 and
10 13.

11 It says, "After we have
12 determined how to draw a valid sample
13 size from the population of interest, one
14 has to determine what clinical endpoints
15 are most appropriate to quantify the
16 exposure effect."

17 On the other side, "After we
18 have determined how to draw a valid
19 sample from the patient population of
20 interest, one has to determine what
21 clinical endpoints are most appropriate
22 to quantify the side effect of the
23 treatment."

24 Do you see that?

1 A. Yes, sir.

2 Q. Those are very similar
3 sentences, correct?

4 A. Yes, sir.

5 Q. Next you have, "For the
6 present legal case," on the other side --
7 in valsartan, you have, "For the present
8 legal case."

9 And on the other side, you
10 have, "For the present legal case."

11 Do you see that?

12 A. Yeah.

13 Q. And then on the valsartan
14 side, you say, "For the present legal
15 case, the endpoint is whether the subject
16 had a certain type of cancer or the time
17 to occurrence of cancer."

18 On the Taxotere side, you
19 say, "For the present case, the endpoint
20 is whether the patient had permanent
21 alopecia or not."

22 Do you see that?

23 A. Yes, sir.

24 Q. So you basically plugged in

1 what's relevant for valsartan on one
2 report and what's relevant for Taxotere
3 on the other report, correct?

4 A. I used the same language.

5 Q. Same framework, correct?

6 A. Yes, sir.

7 Q. On the valsartan side, you
8 say, "Suppose that, based on the sample
9 of 100 patients, at the end of the study,
10 four patients experienced such events."

11 On the other side, you used
12 the same "suppose" identically.

13 "Suppose that based on a
14 sample of 100 patients at the end of the
15 study, four patients experienced such
16 events."

17 Correct? Those are
18 identical sentences, right?

19 A. Yes, sir.

20 Q. Next you say, "Obvious
21 estimate of the event rate for the
22 underlying population is .04 or
23 4 percent."

24 On the Taxotere side, you

1 say, "An obvious estimate of the event
2 rate for the underlying population is .04
3 or 4 percent."

4 Those are exact sentences in
5 each report, correct?

6 A. Correct.

7 Q. Next sentence, "This is
8 called a point estimate."

9 On the Taxotere side, you
10 have, "This is called a point estimate."

11 Those are exact sentences,
12 correct?

13 A. Yep.

14 Q. Next you have, "However,
15 this estimate is based on a sample of
16 patients."

17 On the other -- Taxotere
18 side, you have, "However this estimate is
19 based on a sample of patients?"

20 Those are exact sentences in
21 your Taxotere report and your valsartan
22 report, correct?

23 A. Yep.

24 Q. On the valsartan side, you

1 have, "The true event rate for the entire
2 population may be more or less than 4
3 percent."

4 On the Taxotere side, "The
5 true event rate for the entire population
6 may be more or less than 4 percent."

7 Those are exact sentences,
8 correct?

9 A. Yeah.

10 Q. On the valsartan side, you
11 have, "Different studies generating
12 different samples may find a different
13 proportion of subjects with cancer."

14 On the Taxotere side, you
15 have, "A different study based on
16 different sample may find different
17 proportion of patients that experienced
18 alopecia events."

19 Very similar sentence,
20 correct?

21 A. Yep.

22 Q. Next sentence, you have,
23 "Therefore" --

24 MR. NIGH: And we're going

1 to move onto Page 9 of the
2 valsartan report.

3 BY MR. NIGH:

4 Q. "Therefore, when observing
5 results of a single sample, it is
6 important to attach a level of confidence
7 to the observed point estimate."

8 On the Taxotere report,
9 "Therefore, when observing results from a
10 single sample, it is important to attach
11 a level of confidence to the observed
12 point estimate."

13 Those are exact sentences,
14 correct?

15 A. Yep.

16 Q. On the valsartan side, "This
17 quantitative scientific process is called
18 drawing or making inferences about the
19 true event rate."

20 On the Taxotere side, "This
21 quantitative scientific process is called
22 drawing or making inferences about the
23 true event rate.

24 Those are exact sentences,

1 correct?

2 A. Yep.

3 MR. NIGH: Let's take a look
4 at Paragraph 19. Let's compare to
5 this Paragraph 21 in Taxotere.

6 BY MR. NIGH:

7 Q. Next you have, "Let me turn
8 to the issues of comparing two groups of
9 subjects, one having been exposed and the
10 other being in the control."

11 And on the Taxotere side,
12 "Let me turn to the issues of comparing
13 two groups of patients, one receiving
14 Taxotere and the other receiving a
15 control."

16 Very similar sentences,
17 correct?

18 A. Yep.

19 Q. On the valsartan side, "To
20 make sure that two samples of subjects
21 are comparable with respect to all
22 potential confounders, we often rely on a
23 randomized clinical trial setting."

24 On the Taxotere side, "To

1 make sure that two samples of patients
2 are comparable with respect to all
3 potential confounders, we often rely on a
4 randomized clinical trial setting."

5 Do you see that?

6 A. Yep.

7 Q. Those are identical
8 sentences, correct?

9 A. Yep.

10 Q. And here, in valsartan, you
11 never looked at any clinical trials,
12 whereas you looked at clinical trials in
13 Taxotere, correct?

14 A. I just gave the information.
15 The gold standard to investigate any
16 difference between the two groups would
17 be based on the clinical trial. That's
18 the point.

19 Q. Right. But to try to set up
20 a clinical trial where you expose
21 patients to contaminated --
22 NDMA-contaminated valsartan, compared to
23 patients who are unexposed to -- or not
24 exposed to contaminated valsartan, but

1 given uncontaminated valsartan, to set up
2 a trial setting where you were to give
3 patients contaminated with valsartan as
4 the test group, especially contaminated
5 with levels 200 times over the threshold
6 level set by the FDA, that sort of test
7 would not get approval from any IRB that
8 you know of, correct?

9 A. Well, sir, I think this
10 paragraph is not really ask us to have
11 clinical trials on valsartan case. I
12 just wanted to presenting what is the
13 gold standard, if we can do it.

14 The gold standard is using a
15 clinical trial randomized. If we cannot
16 do it, then we go to the next level of
17 investigation.

18 I just want to point out why
19 the randomized clinical trial gives us a
20 gold -- so-called gold standard.

21 Q. I understand. My question
22 is -- I'm sorry. Did I interrupt you?

23 A. No. No, sir.

24 Q. Okay.

1 A. I'm just trying to explain
2 what your question.

3 You asking me, can we do
4 clinical trials for valsartan case?

5 I think this is -- in my
6 humble opinion, we cannot do that, right.

7 I want to pointed out in
8 Paragraph 19 here, I simply indicate to
9 the judge, or to the court, I said,
10 listen, what is the gold standard if we
11 can do it, which is the randomized
12 clinical trial, right.

13 Q. Well, as --

14 A. But -- sorry, go ahead.

15 Q. Sorry. I didn't mean to
16 interrupt you.

17 As it relates to valsartan,
18 clinical trials would not be a gold
19 standard because it would be unethical to
20 give -- to try to setup a clinical trial
21 that tests whether or not people who are
22 getting contaminated valsartan over a
23 long period of time would get cancer or
24 have an increased risk of cancer compared

1 to control group, because you can't --
2 you wouldn't get -- you wouldn't be able
3 to get approval for that sort of clinical
4 trial, right?

5 A. Right. I don't mean that I
6 said we needed to do it for randomized
7 trials for valsartan case. Just in
8 general, the gold standard is to
9 conduct -- is to conduct a randomized
10 clinical trial. If we cannot do it, then
11 what is the best next level? That's what
12 I'm trying to say.

13 Q. I understand. As it applies
14 to valsartan, though, the gold standard
15 would not be randomized clinical trials,
16 because it would be unethical to conduct
17 such a trial where you're giving
18 people -- you're intentionally giving
19 people NDMA-contaminated valsartan,
20 correct?

21 A. Sir, in that case, what is
22 the gold standard to evaluate valsartan
23 case then? I have no idea what your
24 definition by gold standard.

1 There is no gold standard.

2 If you cannot do randomized trial,
3 there's no gold standard anymore.

4 Q. If you can't do a randomized
5 controlled clinical trial, what would be
6 the next best quality of evidence?

7 A. In my --

8 Q. If --

9 A. Go ahead.

10 Q. Sorry.

11 I added, if you can't -- let
12 me repeat my question.

13 If you can't do a randomized
14 clinical trial, what would be the next
15 best quality of evidence in the hierarchy
16 of scientific evidence?

17 A. For this case?

18 Q. For any case, if you're --
19 if it's unethical to conduct a randomized
20 clinical trial, what would be the next
21 best quality of evidence in the hierarchy
22 of scientific evidence? It would be
23 epidemiological studies, correct?

24 A. Well, I'm not an

1 epidemiologist. I cannot speak for
2 epidemiology. I'm just speak as a
3 statistician. If you're asking me an
4 epidemiology question, I cannot answer,
5 sir.

6 Q. Okay. So as a statistician,
7 you've given this statement that clinical
8 trials are the gold standard.

9 You use that same statement
10 in Taxotere where you're looking at
11 randomized clinical trials. And then you
12 also plug it into valsartan where it's
13 unethical to do clinical trials. So if
14 you can't use clinical trials, do you
15 know the scientific -- hierarchy of
16 scientific evidence would then next state
17 that epidemiological studies would be the
18 next best evidence?

19 A. I would say observational
20 study instead of, quote, epidemiological
21 studies if that's okay with you?

22 Q. That's okay. Observational
23 studies correct?

24 A. Yeah. Yeah. That's what I

1 would say, observational studies.

2 Q. Now, observational studies
3 are oftentimes commonly referred to as
4 epidemiological studies, correct?

5 A. I don't know. If you're
6 using your terminology, it's okay. If
7 you think it's equivalent, that's in your
8 book, I'm saying I prefer to use
9 observational study. Is that okay with
10 you?

11 Q. Yes. All right. Let's take
12 a look at the next sentence. 19, if you
13 can see, "Such a clinical study" -- this
14 is for the valsartan -- your valsartan
15 report.

16 "Such a clinical study
17 yields a well designed experiment that
18 has the potential for generating reliable
19 prospective data on safety."

20 In your Taxotere report,
21 "Such a clinical study yields a well
22 designed experiment that has the
23 potential for generating reliable
24 prospective data on drug efficacy or

1 safety."

2 Those are exact sentences,
3 correct?

4 A. Yes, sir.

5 Q. Next you say, such studies
6 are conducted and monitored according to
7 a pre-specified protocol which details
8 the exposure administered (example, form,
9 dosage, frequency), the clinical and
10 biological endpoint (example, lab value,
11 patient's quality of life, time to
12 remission, time to a toxicity event), the
13 study patient population and other
14 clinical and statistical considerations."

15 In the Taxotere report, you
16 put, "Such studies are conducted and
17 monitored according to pre-specified
18 protocol, which details the treatments
19 administered (example, form, dosage
20 frequency), the clinical or biological
21 endpoints (example, lab value, patient's
22 quality of life, time to remission, time
23 to a toxicity event), the study patient
24 population, and other clinical and

1 statistical considerations."

2 Those are exact sentences in
3 your two reports, correct?

4 A. Yes, sir.

5 Q. Next, in valsartan, you put,
6 "The trial is usually randomized and
7 blinded."

8 On the other side, you put,
9 "The trial is usually randomized, which
10 means patients are assigned randomly to
11 one of the study arms."

12 Very similar start of each
13 of those sentences, correct?

14 A. Looks like different to me.
15 But it's okay if you say similar.

16 Q. Well, your next sentence
17 actually has the second half of the
18 sentence from Taxotere. You put, "Such
19 subjects are assigned randomly to one of
20 the study arms."

21 That's very similar to the
22 end of your Taxotere sentence, correct?

23 A. Yes, sir.

24 MR. NIGH: Then let's go down

1 to the "this avoids."

2 BY MR. NIGH:

3 Q. You put, "This avoids
4 selection bias or other experimental
5 bias."

6 On the Taxotere, "This
7 avoids selection bias or other
8 experimental bias."

9 Those are exact sentences,
10 correct?

11 A. Yes, sir.

12 Q. Your next sentence in
13 valsartan, "When appropriately designed,
14 results from a well conducted randomized
15 clinical trial are regarded as a gold
16 standard in controlled settings to
17 evaluate the efficacy and safety of an
18 exposure."

19 On the Taxotere side, "When
20 appropriately designed, results from a
21 well conducted randomized clinical trial
22 are regarded as a gold standard in
23 controlled settings to evaluate the
24 efficacy and safety of treatment."

1 Those are almost identical,
2 correct?

3 A. Yes, sir.

4 MR. NIGH: Now, let's turn
5 to, in your valsartan report, Page
6 19. Let's look at Paragraph 18 of
7 Taxotere. And let's look at
8 page -- Paragraph 18 of Taxotere
9 and Paragraph 31 in valsartan.

10 BY MR. NIGH:

11 Q. At 31 you say, "Even if we
12 accept Dr. Madigan's criteria with a
13 false positive of .05 as an arbitrary
14 threshold value."

15 And then I want to direct
16 your attention to, "This procedure was
17 generally used to establish the so-called
18 statistical significance of a result when
19 testing a single clinical endpoint in a
20 single study."

21 Do you see that?

22 A. Yes, sir.

23 Q. Then in 18 you put, on the
24 second part of that, after the comma, "Is

1 typically used by a study investigators
2 and statisticians to establish the
3 statistical significance of a report when
4 testing a single clinical endpoint in a
5 single study."

6 Do you see that?

7 A. Yes, sir.

8 Q. Do you see how both of those
9 sentences are similar?

10 A. That's the basic principle,
11 sir. This is a statistical principle.

12 Q. Next, let's have -- sorry.
13 Go ahead.

14 A. This is a basic, like, a
15 textbook language.

16 Q. On 31, the second sentence.
17 "This level can be very liberal, i.e.,
18 can result in statements of statistical
19 significance when none exist, if multiple
20 statistical tests and/or studies are
21 examined simultaneously."

22 On the right side, "The 5
23 percent level of significance for
24 hypothesis testing can be too liberal,

1 can result in statements of statistical
2 significance where none exist if multiple
3 endpoints and/or studies are examined
4 simultaneously."

5 Do you see how those
6 sentences are almost identical?

7 A. Yes, sir.

8 Q. And this is in response to
9 criticizing Dr. Madigan in looking at
10 multiplicity, correct?

11 A. You know, sir, this is very
12 interesting, because Dr. Madigan was the
13 other side for the Taxotere.

14 He actually utilized the
15 same methodology, observational study, in
16 Taxotere.

17 So those two legal cases,
18 Dr. Madigan's reports, yeah, very
19 similar. So we have the similar
20 concerns, right. That's basically -- he
21 is violating the fundamental statistical
22 principles to do his analysis.

23 Q. Let me see if I have this
24 right, because I think what you're saying

1 is his reports look almost identical.

2 But have you looked at the
3 report in Taxotere and looked at his
4 report in valsartan? Have you seen that
5 they're actually very different?

6 A. No, sir. I'm trying to say
7 he used the same statistical principle to
8 analyze both legal cases.

9 And both have had the same
10 problem, a basic fundamental problem,
11 against the statistical principles.

12 So I use the same language.
13 I say, well, in the Taxotere, we already
14 raised the issue. And you didn't answer
15 very well. Why do you want to use the
16 same flawed argument in a new case?

17 Q. Well, it's actually that you
18 commonly criticize experts for not using
19 or looking at multiplicity.

20 This is a common theme
21 across your expert reports. It's not
22 just for Dr. Madigan. We're going to
23 look at Celebrex and we're going to look
24 at several others. You commonly raise

1 the issue of multiplicity, because any
2 time someone is looking at results from
3 single studies, you want to make it a
4 multiplicity issue, correct?

5 MR. MERRELL: Objection to
6 form.

7 THE WITNESS: It's not for
8 me, sir. If you check FDA's
9 principle of drug approval
10 process, they don't allow you to
11 use a single study or multiple
12 endpoint, right, without a
13 multiple adjustment. Right.
14 Everyone knows.

15 And in New England Journal
16 of Medicine recently, saying you
17 cannot reporting so many different
18 P-values, if different endpoint
19 anymore. You know, you can see
20 the latest articles published in
21 New England Journal of Medicine,
22 they don't report P-value
23 repeatedly for primary endpoint,
24 secondary endpoint, or different

1 endpoint.

2 They said no way. You are
3 going to violate the multiple
4 comparison principle. It's not
5 for me -- you know, for me only,
6 sir. It's actually fundamental
7 issue of the statistical methods,
8 right.

9 If you look at so many
10 things all together, and even
11 there is nothing cooking, nothing
12 going on, by chance, if you use
13 the same rule, like a .05 as a
14 threshold value, we actually have
15 lot of misinformative result or
16 misleading conclusions.

17 That's what my point.

18 BY MR. NIGH:

19 Q. All right. Well --

20 A. It's not only for -- it's
21 actually from other agencies. And you
22 can check easily, you know, the FDA's
23 website. The book I cited by Furberg,
24 right, you just mentioned this book,

1 right. Everyone is worried about the
2 multiple comparison issues.

3 Q. Well, I'm glad you raised
4 that. You raised two different
5 references or two different societies,
6 the FDA and The New England Journal of
7 Medicine, correct?

8 A. Yes, sir.

9 Q. Now, aren't you aware that
10 the FDA says that it's improper to use
11 Bonferroni when looking at safety issues?

12 MR. MERRELL: Objection to
13 form.

14 THE WITNESS: I don't know
15 exactly what FDA's principle of
16 looking at safety endpoint with a
17 document or not. I don't know.

18 BY MR. NIGH:

19 Q. Do you recall -- you just
20 told me the FDA when they're looking at
21 the principle of drug approval, that they
22 will use multiplicity. But do you
23 realize the FDA has actually condemned
24 the use of Bonferroni when looking at

1 safety issues?

2 A. Well, I think what I'm
3 trying to say for most NDA, which is new
4 drug applications, FDA insist that we
5 need to apply a multiple -- the
6 adjustment, comparison adjustment.

7 I believe in some trials
8 they use safety endpoint, which is no
9 surprise. For example, you want to study
10 anti-diabetes drug, the heart attack,
11 stroke, CV death are the safety endpoint,
12 right. So in that case, it's a safety
13 endpoint.

14 And I believe FDA also
15 insists that you needed to make
16 adjustment for multiple comparisons.

17 Q. So you're not aware then
18 that the FDA has said that it's improper
19 to use Bonferroni multiplicity testing
20 when looking at safety issues? Do you
21 know one way or the other?

22 MR. MERRELL: Objection to
23 form.

24 THE WITNESS: I said -- sir,

1 anti-diabetes drug, you usually
2 would want to conduct a safety
3 trial to see the anti-diabetic the
4 drug would increase the MI,
5 stroke, or CV death. That's
6 actually the safety endpoint.

7 And for this endpoint,
8 everybody knows what's called,
9 MACE, M-A-C-E, the major
10 cardiology -- cardiovascular
11 event, and we do need a multiple
12 comparison.

13 I believe in FDA's position,
14 they also like to have the
15 multiple comparisons.

16 But for your case, for
17 example, valsartan impurity, I'm
18 not for sure FDA has experienced
19 dealing with this kind of
20 situation yet. It's pretty new,
21 right. So I don't know what their
22 position, is.

23 I cannot speak with FDA. I
24 am not expert in regulatory

1 science. I just use my basic
2 statistical principle to share
3 with you, even for safety
4 endpoint, if you don't take care
5 with the multiple comparison,
6 we're going to have a lot of false
7 positive claims.

8 That means the treatment
9 probably is safe, but because you
10 don't make adjustment, you find a
11 lot of toxicity models.

12 So that's a concern, right.
13 It's not really separated from
14 efficacy endpoint from a safety
15 endpoint. I believe we should
16 apply similar principle to safety
17 and efficacy endpoint altogether.

18 BY MR. NIGH:

19 Q. I understand your opinion is
20 that you should apply multiplicity to
21 safety endpoints. I'm not asking you
22 about that.

23 You raised the FDA as one of
24 your references. I'm now asking you

1 about the FDA and Bonferroni
2 specifically.

3 Hasn't the FDA weighed in,
4 or are you aware of whether or not the
5 FDA has weighed in on whether or not it's
6 inappropriate to use Bonferroni when
7 looking at safety issues?

8 A. I don't know, sir. We've
9 already explored the Bonferroni
10 adjustment has been used by FDA
11 regulatory people. We can find out.

12 Q. But I'm here today asking
13 you. You raised FDA, and I'm here today
14 asking you about your opinions.

15 You haven't seen anything
16 where the FDA says it's okay to use
17 Bonferroni for safety issues, correct?

18 MR. MERRELL: Objection to
19 form.

20 THE WITNESS: Well, I said
21 it for antidiabetes drug, they may
22 use a safety endpoint. That's one
23 example.

24 BY MR. NIGH:

1 Q. In terms of the New England
2 Journal of Medicine, have you seen
3 multiple studies that have criticized
4 using Bonferroni adjustment for safety
5 issues?

6 MR. MERRELL: Objection to
7 form.

8 THE WITNESS: I cannot speak
9 with New England Journal of
10 Medicine. They just issue a
11 guideline for statistical
12 analysis. They said, well, all
13 the endpoints. They didn't say
14 efficacy or safety endpoint by the
15 way, which we can go on the
16 website and look, right, to look
17 at carefully.

18 They are simply saying,
19 look, you have one study, you have
20 to tell me for primary endpoint
21 which is safety or efficacy.

22 I don't know exactly the
23 language they use. But they say
24 for primary analysis, you utilize

1 the P-value. Pre-specify the
2 level you want it to. Then the
3 next level for secondary endpoint,
4 you are not allowed to apply the
5 same principle, .05 anymore to
6 claim for the secondary endpoint,
7 there is issue or not. That's my
8 understanding.

9 BY MR. NIGH:

10 Q. I'm sorry, it's your
11 understanding that for a secondary
12 endpoint that The New England Journal of
13 Medicine says that you're no longer
14 allowed to apply .05 for as your P-value
15 for the secondary endpoint. That's your
16 testimony?

17 MR. MERRELL: Objection to
18 form.

19 THE WITNESS: They don't --
20 they don't allow you to report in
21 the P-value anymore.

22 BY MR. NIGH:

23 Q. Okay. But when they report
24 as the secondary endpoint, they still

1 show the confidence intervals for those
2 secondary endpoints at a 95 percent
3 confidence interval. Right?

4 A. Yeah, the confidence
5 interval contains more information than
6 the P-value --

7 Q. Right.

8 A. -- the size difference.

9 Q. But the confidence interval
10 reflects the P-value. In other words, if
11 you can see in that confidence,
12 95 percent confidence interval that it
13 doesn't cross one, then you know you have
14 a P-value less than .05, correct?

15 A. Well, if you want to
16 interpret it that way, you can do that.
17 But confidence interval would provide you
18 more information than across the
19 boundary, null value or not, right? You
20 can tell me how big the confidence
21 interval is. If it's too wide, you know
22 you don't have enough information to tell
23 the truth, right?

24 If the size of the estimate,

1 like in this case, odds ratio or relative
2 risk is very small, you say, well, you
3 know, you have a large trial and
4 thousands, thousands of patients in
5 cardiovascular trial, right. And no
6 matter what, how low your odds ratio,
7 like 1.01, you still have a statistical
8 significance. Your confidence interval
9 still excluded here, one, for example,
10 odds ratio, but the question is, is that
11 really interesting physically or
12 clinically speaking. Right? That's
13 confidence interval will tell you, right.

14 It's much more information
15 than just simply P less than .05.

16 Q. Okay. When I asked you
17 about multiplicity and Bonferroni, you
18 raised FDA and you raised New England
19 Journal of Medicine. I'm only talking
20 now for this question, multiplicity and
21 the use of Bonferroni.

22 Do you believe the FDA and
23 The New England Journal of Medicine
24 support the use of Bonferroni as when it

1 comes to safety issues?

2 A. Sir, I give you one example
3 for MACE event. I do understand, I
4 repeat it three times for you. That's a
5 safety endpoint.

6 Q. Have you --

7 A. Do you understand what I'm
8 trying to say, sir? I mean --

9 Q. I do.

10 A. -- it's a MACE -- okay.

11 So why don't you take that
12 example and if we actually can get the
13 FDA, being the review for the past five
14 years, let's think about how many FDA is
15 concerning about the safety endpoint,
16 right. How do they handle the safety
17 endpoint. But I don't know the detail at
18 all, right.

19 I am just sharing with you,
20 sir, based on my experience dealing with
21 FDA, they don't want us to apply P less
22 than .05 for every endpoint.

23 I don't know if they
24 restrict at the efficacy endpoint and

1 they don't care about the safety
2 endpoint, I don't know their positions,
3 sir. This is a principle we do.
4 Personally, as you know well, I set up
5 for safety and efficacy endpoints
6 together. We need it to be helpful,
7 right. Don't make a large, very large
8 unacceptable false positive rate.

9 For example, let me give
10 one -- ten seconds, give you one example.
11 If you have three studies, right,
12 independent study, if you apply the P
13 less than .05, clearly there is an issue,
14 right.

15 Then apply the three
16 clinical trials independently, the false
17 positive rate will become 14 percent
18 instead of 5 percent anymore.

19 I say well, do you really
20 think 14 percent is acceptable to be the
21 false positive rate, which to me is very
22 high, right.

23 You can apply the safety
24 endpoint here too. If you say three

1 studies, study the efficacy issue, well,
2 let's apply .05 for each study. If there
3 is study, P-value less than .05, then
4 let's be clear, there is a safety issue.

5 I said, sir, wait a second,
6 if you apply this principle, you are
7 going to make a mistake. 14 percent
8 is -- 14.5 percent by the way, okay, to
9 make a mistake. Claim something unsafe.
10 But actually the drug is safe.

11 Do you think that's
12 acceptable? If you think acceptable, or
13 society, or FDA accept it. Well, I have
14 no argument, that's their position,
15 right. I just share with you my
16 experience with FDA and also New England
17 Journal of Medicine.

18 Q. I'm not asking about, you
19 know, just multiplicity issues at this
20 point. My question is simply Bonferroni
21 now for this question.

22 Are you aware that the FDA
23 has criticized the use of Bonferroni when
24 looking at multiplicity issues?

1 A. FDA, I don't think that they
2 criticize using Bonferroni, right.
3 Bonferroni may be applicable to efficacy
4 endpoint and they probably little bit of
5 liberal for the safety.

6 But my point is that I don't
7 know how liberal you want allow safety
8 say, well, forget about any adjustment.

9 By the way, Bonferroni
10 adjustment is just one adjustment. You
11 can have other adjustment. You don't
12 have to stay with Bonferroni adjustment.

13 The principle is a multiple
14 comparison issue. Do you think that
15 there is a problem applied the same rule
16 for every single endpoint for every
17 study, right, with the same P less than
18 .05. I said well, be careful. This
19 could be a lot of misleading conclusions.
20 That's what I'm trying to say, right.
21 Nobody would argue with me. You cannot
22 do that. Even Dr. Madigan cannot
23 dispute, say, well, there is a higher,
24 much higher unacceptable false positive

1 rate if you don't take care of multiple
2 comparison problem. He just argue, say,
3 well, maybe for safety you can relax a
4 little bit. The question is how much
5 relaxation you are waiting to do for
6 safety endpoint, right. We don't know.

7 You know, you can ask Dr.
8 Madigan's opinion. Do you think he say,
9 well, forget about any adjustment. Just
10 stay with .05, for anything, for safety.
11 Do you think that is okay or it is not
12 okay? Well, I'm not in position to
13 educate Dr. Madigan. He knows this very
14 well.

15 Q. I didn't ask you about
16 Dr. Madigan. I simply -- and you gave me
17 a lot of information that I didn't ask
18 about.

19 So what I asked was, are you
20 aware that the FDA has criticized the use
21 of Bonferroni when looking at
22 multiplicity issues related to safety.

23 MR. MERRELL: Objection to
24 form.

1 THE WITNESS: I think FDA
2 would ask us to make multiple
3 comparison adjustment. Bonferroni
4 just one of the tool to make
5 adjustments, sir. Okay. If
6 you --

7 BY MR. NIGH:

8 Q. I think --

9 A. Specifically if you want to
10 put your words in my mouth, if you think
11 FDA against to using Bonferroni
12 adjustment, I say no, they don't have any
13 document saying that you cannot use
14 Bonferroni adjustment.

15 If you have some document
16 issued by FDA saying Bonferroni
17 adjustment is no good, I will be willing
18 to learn. Everyday I learn something
19 brand new, which is nothing new to me,
20 right. We should learn something new.

21 So if you say somebody
22 saying, FDA saying no, you shouldn't do
23 Bonferroni adjustment at all for safety.
24 That's fine. That's their opinion,

1 right.

2 I said, well, look, whatever
3 you want to claim, that's regulatory
4 agency's claim. I just speak for myself.
5 I say, well, my experience with FDA they
6 want to make multiple comparison
7 adjustment.

8 But you say, are they
9 against using Bonferroni. I said well,
10 where is any document. They say we don't
11 like Bonferroni adjustment for safety
12 endpoint. If you have this document I'd
13 be very happy to read it, sir.

14 Q. It sounds to me from that
15 answer that you're not aware of any
16 document or any situation where the FDA
17 has criticized the use of Bonferroni when
18 looking at safety issues; is that
19 correct?

20 A. Well, that's my knowledge.
21 I don't know where and when the FDA has
22 this issued such a statement or position,
23 right. I don't know, sir.

24 Q. Now let's take a look at --

1 let's talk about New England Journal of
2 Medicine. Are you aware of studies that
3 criticize the use of Bonferroni when
4 looking at safety issues?

5 MR. MERRELL: Objection to
6 form.

7 THE WITNESS: I don't know
8 offhand right now any paper they
9 criticize. I think the best way,
10 we can go to the website of New
11 England Journal of Medicine,
12 right. They have so-called
13 guidance for statistical analysis.

14 I know most associate
15 editors of statistics in New
16 England Journal of Medicine, they
17 all my colleagues at Harvard,
18 right, so we can easily get their
19 opinion and say what is the
20 position of New England Journal of
21 Medicine, right.

22 But first, sir, you can
23 Google their website. They have
24 clearly stated what we should do

1 from now on handling this
2 secondary endpoint.

3 Like you said very well, we
4 use confidence interval, insert a
5 P-value, right. I think that is
6 one step improve our scientific
7 investigation.

8 The P-value is useless
9 information for us. Maybe pass
10 the first hurdle. But then after
11 pass the first hurdle, you ask
12 yourself, how do you interpret
13 clinical utility of your findings,
14 right, instead of telling me the
15 P-value is .04.

16 BY MR. NIGH:

17 Q. My question, was let's talk
18 about The New England Journal of
19 Medicine. Are you aware of studies in
20 The New England Journal of Medicine that
21 criticize the use of Bonferroni when
22 looking at safety issues?

23 MR. MERRELL: Objection to
24 form.

1 THE WITNESS: So I said many
2 times, I don't have the paper
3 right now I can show that to you.
4 But the best way to go into the
5 website to look for the guidance,
6 right.

7 BY MR. NIGH:

8 Q. It sounds to me like you're
9 not aware of any journal articles or
10 studies in The New England Journal of
11 Medicine that criticize the use of
12 Bonferroni when looking at safety issues;
13 is that correct?

14 A. Well, I don't know any paper
15 I know. But I'd be happy to learn.

16 Q. When you put your expert
17 report together, where you insisted upon
18 the use of Bonferroni for the data in
19 valsartan, did you do any research to see
20 whether or not that has now been
21 criticized in journal articles, or by
22 regulatory agencies when looking at
23 safety?

24 MR. MERRELL: Objection to

1 form.

2 THE WITNESS: Well, that was
3 not in my assignment. As you
4 noted very well, in several of my
5 reports, in the legal cases, I
6 raised the same issue, right. I
7 said well, be careful to interpret
8 the safety issue. Because this
9 multiplicity.

10 I don't think Bonferroni is
11 really important role here.
12 Bonferroni is just one of the
13 tools. If we are smart enough, we
14 can figure out another way to make
15 adjustments, right. Not using
16 Bonferroni adjustment.

17 Bonferroni adjustment some
18 people say maybe a little bit
19 conservative. I say well, that's
20 okay. Some say you have a way to
21 make adjustment for multiple
22 comparison, please do it, right.
23 At least so we can see it.

24 And instead of a one-way

1 street, don't make any adjustment.

2 For me that's not very good.

3 BY MR. NIGH:

4 Q. You commonly raise
5 Bonferroni as your go-to multiplicity in
6 many of your expert reports, correct?

7 A. Yeah. That's the obvious
8 way, straightforward way to handle
9 multiple comparisons, sir.

10 Q. Well, actually false
11 discovery rate is used much more often.
12 False discovery rate computations are
13 used much more often when looking at
14 safety issues than Bonferroni, correct?

15 A. I don't know much about
16 discovery rate, sir. That's another
17 school of thought. And I think that they
18 are essentially equivalent to using
19 P-value. Just using different scale.

20 Q. And also Fisher pooling is
21 one of the more -- much more common ways
22 of looking -- or looking at multiplicity
23 across clinical studies, correct?

24 A. No, sir --

1 MR. MERRELL: Objection --

2 MR. NIGH: Sorry. Let's
3 strike that question. Sorry.
4 Strike that question, please.

5 THE WITNESS: Okay.

6 BY MR. NIGH:

7 Q. And also Fisher pooling is
8 used much more often when looking at
9 safety issues than Bonferroni, correct?

10 A. No, sir. You misunderstand
11 Fisher pooling P-value now. Fisher
12 P-value pooling is very similar to
13 meta-analysis. They have several
14 studies, each study has a P-value. They
15 wound up pooling that P-value across
16 several studies, getting a global
17 P-value. Okay. So that's similar to
18 methodology now.

19 So the -- you raise the
20 multiple comparison, is not really
21 similar to meta-analyses.

22 So, I'm sorry, I probably
23 missed your point. But a pooling,
24 Fisher's pooling is quite different

1 compared with multiple comparison
2 problem.

3 Q. Fisher pooling allows you to
4 look at the rates of effect across a
5 collection of studies, correct?

6 A. Yeah. That meta-analysis,
7 essentially.

8 Q. It's similar to a
9 meta-analysis, correct?

10 A. Yeah. So it is orange and
11 apples you are talking about here now,
12 right. Before you are talking about
13 multiple studies looking individually.
14 Now you say wait a minute, let me pool it
15 all together now. That's a different way
16 to answer your question, right.

17 Q. Those are both -- those are
18 both ways to look at false positive rate.
19 You can look at Fisher pooling across a
20 pool of studies to look to see if that
21 Fisher pool rate still shows an effect
22 for the question and answer, correct?

23 A. That's a meta-analysis, sir.

24 Q. Now, you didn't choose to do

1 a false positive rate in your opinion at
2 all, correct?

3 A. No. Because it didn't
4 matter considering the discovery rate.
5 My assignment is not really creating new
6 animals for you guys to evaluate, right.
7 So I stay with the P-value Dr. Madigan
8 used.

9 Q. My problem here, I actually
10 worded the question wrong.

11 You didn't choose to do a
12 false discovery rate in your opinion at
13 all, correct?

14 A. Because Dr. Madigan didn't
15 do that either.

16 Q. In fact, you chose the most
17 conservative or what has been widely
18 criticized for safety issues as the most
19 conservative approach for multiplicity,
20 for measuring multiplicity, correct?

21 MR. MERRELL: Objection to
22 form.

23 THE WITNESS: Sir, I
24 don't -- I don't understand your

1 language. Why do we criticize the
2 Bonferroni adjustment? What is
3 the -- what are you talking about,
4 why are you criticize?

5 BY MR. NIGH:

6 Q. Sir, again, you haven't
7 reviewed any studies that criticize using
8 Bonferroni? Not even just in the New
9 England Journal of Medicine. But that
10 criticize using the Bonferroni adjustment
11 when looking at multiplicity issues. You
12 haven't reviewed studies on that in
13 regards to safety?

14 A. Well, sir, you have a
15 different school of thought, right, in
16 statistics even. This is like your legal
17 profession. There are so many different
18 ways to actually make a decision, right.

19 People have a different way
20 to make adjustment for multiple
21 comparisons.

22 You know, Bonferroni is one
23 of this, right. Obvious,
24 straightforward, commonly used adjustment

1 tool. You can use the other adjustment,
2 right, if you wanted to.

3 I just choose one to
4 illustrate, this can be problematic if
5 you don't make multiple adjustment. So
6 my point is that multiple comparison
7 adjustment, I'm not to say you should
8 have used always a Bonferroni adjustment.
9 If you don't like Bonferroni adjustment,
10 you can use alternative way.

11 But the question is, should
12 the way take care of multiple comparison
13 problem or not. That's the issue.

14 Q. Right. You chose, in terms
15 of your example, Bonferroni, which would
16 actually be the most conservative way of
17 looking at multiplicity, a/k/a, the
18 friendliest measure to pharmaceutical
19 companies when it comes to looking at
20 safety issues, right?

21 A. I'm not for sure when you
22 say conservativeness, this is just one of
23 the tools, sir. I repeat it so many
24 times. I said you don't have to use

1 Bonferroni adjustment. My point is you
2 have to make some adjustment. I just
3 give you example.

4 If you use Bonferroni
5 adjustment, then what kind of threshold
6 value you should use, right. If you have
7 a smaller smarter way to handle multiple
8 comparison problem, I have no issue, sir.
9 At least you have to address this issue
10 of multiple comparison, right. It
11 doesn't matter if it is an efficacy
12 endpoint or safety endpoint, right. Both
13 are very important to us. You don't want
14 to criticize the impurity in valsartan
15 has some issues.

16 If you look at 100 studies,
17 just happen to say one study show up with
18 a P-value less than .05, you say wow,
19 look, this is evidence. It can be
20 helpful to interpret this, right, because
21 you're looking so many studies both
22 together, right.

23 If you stay with the same
24 rule for each study, you are going to

1 make some wrong conclusions. That's what
2 I said in my report.

3 I didn't say you have to use
4 Bonferroni. I just say if you use the
5 Bonferroni, this is the threshold value
6 you should use, right.

7 If you disagree with this
8 approach, that's fine. But my point is
9 you should make some adjustment, right.

10 Q. The example that you give in
11 many of your expert reports, Bonferroni,
12 would actually be the most conservative
13 way of looking at multiplicity, a/k/a the
14 friendliest measure to pharmaceutical
15 companies when it comes to looking at
16 safety issues, correct?

17 MR. MERRELL: Objection to
18 form.

19 THE WITNESS: Well, I'm not
20 quite sure if this is most
21 conservative way to do it. I
22 don't know. Maybe. But I'm --
23 will be very happy to learn what
24 is alternative way to dealing with

1 your present case, right, handling
2 multiple comparisons.

3 BY MR. NIGH:

4 Q. Have you not seen numerous
5 studies talking about using false
6 discovery rates instead of Bonferroni
7 when discussing safety issues?

8 A. Well, there are some. But
9 again, I said before, sir, Dr. Madigan
10 didn't use discovery rate. So he used
11 the P-value, right. So my assignment say
12 could you actually review what
13 Dr. Madigan did in his report. That's
14 what I'm responding to the report.

15 I'm not -- I was not in the
16 position to create another quantity for
17 discovery rate. And because Dr. Madigan
18 didn't use it, why should I bother to go
19 to that route.

20 Q. Well, what you've done is
21 you've cherry-picked the most
22 conservative measure, Bonferroni, when
23 looking -- as an example, when looking at
24 multiplicity issues. And this is the

1 same cherry-picking you've done for many
2 of your past expert reports, just looking
3 at Bonferroni as opposed to other
4 measures of multiplicity.

5 MR. MERRELL: Objection to
6 form.

7 THE WITNESS: I strongly
8 disagree with your word
9 "cherry-picking." I didn't look
10 at the data to choose my
11 procedure, right. That's what you
12 call cherry-picking.

13 I actually -- before I even
14 had Dr. Madigan report, I said you
15 should make some adjustment.
16 Bonferroni is one of the tool,
17 right. That's not a cherry-pick
18 answer. That's pre-specified,
19 right.

20 If you disagree with me
21 about Bonferroni adjustment,
22 that's fine. Nobody said that you
23 cannot do that.

24 My point in my report, I say

1 you need to make some adjustment
2 for multiple comparison. If you
3 can show us through the discovery
4 rate to say, oh, this is a better
5 way to make adjustment, I say
6 fine, let's look at it, right.
7 Present it to us. We're going to
8 look at it.

9 BY MR. NIGH:

10 Q. You gave an example earlier
11 where you talked about three studies, and
12 if there was a, you know, P-value of .05.

13 And you said your chances of
14 getting one out of those three studies
15 would be 14 percent. Do you remember
16 that example?

17 A. Yes, sir. It's in my report
18 by the way.

19 Q. Right.

20 What are the chances of two,
21 if two of the three had a positive
22 finding, what would those chances be?

23 A. Oh, it's very easy to do.
24 It's 1 minus .95 times .95. If you had a

1 calculator, you can do very quickly.

2 Q. Right. When you're looking
3 at more than one positive rate, there's a
4 way to calculate that fairly quickly,
5 right?

6 A. Yeah.

7 Q. Okay. It's no longer
8 14 percent at that point, correct?

9 A. Yeah. If you have two
10 studies, I don't know, it's maybe
11 10 percent instead of 5 percent, right.
12 If you have four studies, then suddenly
13 it become 20 percent, right. So the more
14 study that you're looking at, the higher
15 the positive rate now.

16 Q. Right. But you're telling
17 me right now -- I mean two positive
18 results. I'm not talking about one
19 positive out of three. Two positives out
20 of three.

21 Wouldn't that be important
22 to measure, that -- if you had two out of
23 three, that's a different measurement
24 than one out of three in terms of

1 measuring the effect, though, right?

2 A. Yeah, that's a fair --
3 that's a fair question. But my position
4 is not really say out of the three there
5 are two truly positive result, right,
6 supposedly.

7 Now, you are asking me, say,
8 what is the point error now. This is a
9 very interesting question now, right.
10 You say well, your null hypothesis go
11 along with -- the three trials are really
12 -- are not null, right, meaning there's
13 no difference between the two groups. I
14 said, well, at least the one guy, he's
15 talking it up, he's saying what is the
16 chance, I say 14 percent. Then you said,
17 what is the chance if two guys popped up.
18 I don't know. We have to sit down and
19 figure this out.

20 Q. Right. When you're looking
21 at Bonferroni, Bonferroni is focused, in
22 terms of its math and its ideals, when
23 thinking about one false positive out of
24 a collection of studies, correct?

1 A. Yeah. At least one. You
2 pop it up, you claim positive.

3 Q. But when there's two or
4 more, that's one of the main criticisms
5 of Bonferroni, is that dividing the
6 P-value by the number of studies, when
7 there's two or more positive findings,
8 would cause Bonferroni to be much too
9 conservative, right?

10 A. Sir, you actually changing
11 the questions now, right.

12 My point I say in my report,
13 I said it would be helpful when you're
14 dealing with multiple studies, multiple
15 endpoints, to help with multiplicity
16 issue.

17 I give you one example. I
18 said, well, if there is no difference
19 across all the studies, all the
20 endpoints, right, what is the chance
21 you're going to claim something is
22 positive. I said this is the number,
23 right. But if you say wait a minute, I'm
24 changing my story now. I say out of

1 three study, I have two positive, more
2 than .05, then you're asking me, say hey,
3 what is the false positive rate now. You
4 know, that change the story now, right.

5 You can go on forever. You
6 can say three positive out of three, that
7 is a different story now. That is not
8 exactly what I said in my report.

9 Q. I understand it's not what
10 you put in your report. You gave the
11 hypothetical of one out of three.

12 My point is, when it's two
13 out of three, it changes the findings
14 dramatically, it's no longer 14 percent.
15 It's much, much higher -- I mean much,
16 much lower that those chances would
17 happen, that you'd get two out of three
18 by chance when the P-values -- two out of
19 three studies have a P-value of less than
20 .05. That'd be much lower than 14
21 percent, correct?

22 A. Yeah, that's a fair thing to
23 say, yes.

24 Q. In fact, you can do it off

1 the top of your head, but that would
2 actually be much less to get two out of
3 three that are .05 or less, that -- that
4 chances of that pool would actually be
5 less than .05?

6 A. I don't know the
7 mathematics, sir. You are too smart for
8 me to calculate it so quickly. I don't
9 know.

10 Q. Well, when you're looking at
11 a rare event, and most of the -- when
12 you're looking at a rare event of
13 something less than .05 and most of the
14 events in a pooled data are coming up
15 positive as that rare event, in that
16 study, we know then that the -- when you
17 calculate a pool of data, that it's going
18 to be lower than the initial .05, right?
19 I mean that's just a general statistic,
20 general statistics statement.

21 A. Yes, you are absolutely
22 right. If everything go to the direction
23 you like, right, you're combining several
24 studies, of course, you can enhance your

1 argument. Unfortunately, if you look at
2 all the meta-analysis Dr. Madigan cited,
3 on the left-hand side, right-hand side of
4 null value, right, back and forth, back
5 and forth. And it turns out the odds
6 ratio is really not that interesting,
7 1.2, you know, something lower than 2,
8 and, you know, that's the issue, right.
9 You're combining the negative study with
10 a positive study, hopefully the positive
11 study will dominate in your result. You
12 know, people can play all kinds of games,
13 right. I mean, it's unfortunate, right.

14 Q. You know, right now I wasn't
15 asking about Madigan's report. But it's
16 interesting that you brought that,
17 because you just brought up the
18 meta-analysis.

19 Let's set gastric cancer
20 aside in terms of the dietary studies.
21 Let's actually focus on lung cancer.

22 Did you have an opinion on
23 the lung cancer dietary studies?

24 A. Can you show me the report

1 so I can refresh my memory?

2 Q. Well, lung cancer had an
3 effect size of 3.1, P-value of less than
4 .001 in the De Stefani study. Goodman,
5 for men, had an effect of 3.3, P value of
6 .006 for males. For females, Goodman had
7 an effect size of 2.7, .004. And then
8 for Lowe, effect size of 1.1, P-value of
9 .6.

10 So can't you look at that
11 data and immediately realize that the
12 pooling of that data would be less -- a
13 P-value of less than .05?

14 A. You are putting all the
15 study together you're saying, sir?

16 Q. Yes. For lung.

17 A. Are they -- sorry, are they
18 pretty much in a similar population or
19 are they different population?

20 Q. Well, do you know?

21 A. Sorry, sir?

22 Q. Do you know?

23 A. Say it again?

24 Q. Do you know?

1 A. I don't -- I don't know.
2 You just raised the issue. I didn't
3 raise it, you know, saying that checking
4 every study they are similar or not. The
5 meta-analysis are combining.

6 First thing you need to say,
7 well, you know, they are combinable,
8 right. Some actual studies it is not
9 combinable. So -- but people actually
10 just are lumping all the orange and
11 all -- the apples altogether, right,
12 getting a summary of statistics. And
13 using that summary of statistics in a not
14 right way in my opinion, right. So you
15 can combine it any way you want it to.

16 The things that are if you
17 have any negative trial for lung cancer,
18 yes, you do have, right, but if you are
19 only picking up the highly significant
20 event reporting to us, I don't know.
21 Because Dr. Madigan didn't show all the
22 negative trials in the lung cancer,
23 right.

24 Q. I'm sorry, do you believe

1 there is another study that is negative
2 for dietary studies for lung cancer other
3 than what he reported?

4 A. You just said -- the last
5 one, 1.1 or some alteration, you just
6 told me.

7 Q. You give that a negative,
8 that's still an increase, it's more than
9 one, correct?

10 A. Sorry, sir. Using the
11 P-value of what, .6, something like that?

12 Q. .6. Yeah, 1.1 is still an
13 increased risk.

14 A. Oh boy, I tell you, you
15 mixed the fundamental issue about the
16 inference of statistics, right. You
17 cannot say my point estimate is 1.1, I've
18 got a problem, right. Besides you have
19 those observational study, 1.1 odds ratio
20 can be easily changed to less than one if
21 you use different confounders in
22 adjustment. Everybody knows that.

23 You have measurable
24 confounders. If you just happen to

1 measure those confounders, suddenly odds
2 ratio could be .8, .7. So the very low
3 odds ratio really doesn't carry too much
4 weight, right.

5 That's why -- you guys have
6 a very interesting book. I know you know
7 this book very well. Called scientific
8 evidence, right, for lawyers, something
9 like that.

10 In that book, actually it is
11 written by a lawyer actually many years
12 ago. He say, okay, this is our Bible. I
13 look at it, it's very interesting.

14 If the odds ratio is less
15 than two, the guy said forget it, I'm not
16 interested. I ask the lawyer, hey, why
17 are you using the threshold number two?
18 I said, listen, this is observational
19 study is all messed up already. You make
20 all kinds of adjustment. If you use a
21 different adjustment, if we can lower
22 odds ratio point estimate like you say,
23 1.1, right, I can easily swing around,
24 right.

1 But if you have like five or
2 six odds ratio, then we don't have the
3 problem of robustness of your data. This
4 actually, sir, this is the first
5 principle of the so-called Bradford Hill
6 criterion, right, for causation.

7 First one is that you need
8 to worry about the size of effect. Not
9 just like the P-value, right.

10 Q. You referred to it as a
11 negative study, that's why I asked you,
12 but negative would mean below one, in
13 terms of effect size when it comes to
14 statistics, correct?

15 A. I would say it's a neutral
16 study. It's not really called a
17 negative.

18 Q. That's the reason I raised
19 it. I don't disagree with you about the
20 amount of rate -- amount of weight to be
21 given to the effect size. I raised it
22 because you used the word "negative
23 study," right?

24 A. Okay, sorry. I apologize.

1 I use a negative word.

2 Q. 1.1 is technically an
3 increased risk, not statistically
4 significant in the study but it's still
5 technically an increased risk, correct?
6 I'm not talking about what inference to
7 be drawn from it.

8 A. Well, if you don't have an
9 inference, then we just go home today.
10 You don't have to worry about anything
11 anymore, right. Everything based on
12 point estimate, you make a decision, you
13 say wow, is that okay, judge. You can
14 ask the court.

15 Q. So you have three studies.
16 One is a 1.1 increased risk, not
17 statistically significant.

18 The De Stefani 3.1, more
19 than a doubling of the risk statistically
20 significant with a P-value of less than
21 .001. And the other one, 3.3 increased
22 risk effect size with the P-value of
23 .0006.

24 You take those three

1 studies, how do you view those three
2 studies together?

3 A. How do I -- how do I do
4 that?

5 Q. Yes. How do you view those
6 three studies together?

7 A. If I -- if I truly believe
8 those studies are well conducted and they
9 considered all the confounders,
10 adjustment, and it's a prospective -- now
11 be careful of the word "prospective,"
12 right, it's not a risk factor. Okay?
13 Then I would say, yes, there's some
14 strong signal to show us, right, for this
15 case.

16 I don't believe those
17 studies are prospective. Maybe I'm
18 wrong. But if my memory tells me they
19 were not prospective. Okay.

20 Q. You don't believe that the
21 De Stefani or Goodman studies were
22 prospective studies?

23 A. Say it again, I'm sorry,
24 sir.

1 Q. You don't believe that the
2 De Stefani or the Goodman -- the De
3 Stefani lung dietary study and the
4 Goodman dietary study that Dr. Madigan
5 cited, you don't believe that those were
6 actually prospective studies?

7 A. Well, we can check easily.
8 If you put on the papers on the screen we
9 can look very carefully --

10 Q. I'm asking you -- you viewed
11 these studies. I'm asking you your
12 knowledge, before we look at the studies,
13 you don't believe that those were
14 prospective studies?

15 A. Well, I cannot say yes or
16 no. But we can easily check.

17 Q. How about colorectal cancer.
18 You get a study that shows 2.1 increased
19 risk. You get another study that shows
20 1.5 increased risk, P-value of .001, and
21 another study that shows 1.4 increased
22 risk, P-value .005.

23 How do you compare those
24 studies as a pool of studies?

1 MR. MERRELL: Objection to
2 form.

3 BY MR. NIGH:

4 Q. Those results?

5 A. I would -- I would say the
6 same thing, sir. It is well conducted,
7 well balanced with a start of baseline
8 factors, prospectively I then would agree
9 with you, there is some signal indicated,
10 there is a chance the incidence increase,
11 right.

12 Q. Okay. Let's go back to the
13 two studies, I mean the two reports on
14 the screen.

15 Okay. We were in Number 31.
16 And I draw your attention down to using
17 the 5 percent rule. If we can go down to
18 Taxotere on the right side using the
19 5 percent rule. Yep.

20 On the valsartan side, you
21 put "Using the 5 percent rule for
22 claiming statistical significance to
23 analyze simultaneously a large number of
24 tests in a study will yield a high rate

1 of false positive findings." On the
2 right side, you put "Using the 5 percent
3 rule for claiming statistical
4 significance to analyze simultaneously a
5 large number of safety endpoints in a
6 study will yield a high rate of false
7 positive findings."

8 Those are identical
9 sentences in the two reports, correct?

10 A. Yes, sir.

11 Q. Next it says, "Often the
12 overall false positive rate could be as
13 high as 20 percent or more. That is, a
14 very high chance of finding an exposure
15 is not safe with respect to control when,
16 in fact, there is no difference between
17 the two groups."

18 Let's take a look at
19 Number 32. You have -- and let's go to
20 Paragraph 19 for Taxotere. "A standard
21 procedure to handle the multiple
22 comparison issue is to use the Bonferroni
23 adjustment."

24 That's what you put in

1 valsartan.

2 And in Taxotere you put "A
3 standard procedure to handle the multiple
4 comparison issue is to use the Bonferroni
5 adjustment."

6 Those are identical
7 sentences, correct?

8 A. Yep.

9 Q. Next you put, "For example
10 if there are 50 different types of tests
11 conducted, the false positive rate is
12 5 percent, then for each individual test
13 we should use a false positive rate of
14 .1 percent, 5 percent divided by 50, to
15 assess whether there is a potential
16 signal on the safety issue" -- "safety
17 concern."

18 On the other report you put,
19 "For example, there are 50 different
20 types of adverse events considered in the
21 trial. If the total false positive rate
22 is 5 percent, then for each individual
23 adverse event we should use a false
24 positive rate of .1 percent, 5 percent

1 divided by 50, to assess whether there is
2 a potential safety" -- "there is a
3 potential signal on the safety concern."

4 Those are identical
5 sentences, correct?

6 A. Yep.

7 Q. I'm sorry, I missed the very
8 first sentence, which says, "A standard
9 procedure to handle the multiple" -- oh
10 no. We went over that.

11 Next is "The corresponding
12 confidence interval level should be
13 99.89 percent, which is 100 percent minus
14 1 percent" -- or ".1 percent."

15 And on the other report you
16 say, "The corresponding confidence
17 interval level should be 99.9 percent
18 (100 percent minus .1 percent.)"

19 Those are identical
20 sentences, correct?

21 A. Yes, sir.

22 Q. Turning to Paragraph 33, and
23 Paragraph 20, the next paragraph. The
24 next paragraph in valsartan, and then the

1 next paragraph in Taxotere.

2 Next you have "The problem
3 of inflation of a Type I error or
4 positive" -- "false positive rate becomes
5 much worse when we examine the results of
6 several independent clinical studies at
7 the same time with a Type I error rate of
8 .05 for each study."

9 In Taxotere you put "The
10 problem of inflation of a Type I error or
11 false positive rate becomes much worse
12 when we examine the results of several
13 independent clinical trials of the same
14 type with a Type I error rate of .05 for
15 each study."

16 Those are identical
17 sentences, correct?

18 A. Yep.

19 Q. In valsartan you put "For
20 example, suppose there are three
21 independent studies which compare the
22 exposure group with control."

23 In Taxotere you put "For
24 example, suppose there are two

1 independent studies which compare
2 Taxotere."

3 Do you see that?

4 A. Yep.

5 Q. Similar but you've gone to
6 three in valsartan instead of two in
7 Taxotere, correct?

8 A. Sorry, sir, I missed what
9 you are saying.

10 Q. I said similar sentences
11 except for you've gone with three in your
12 hypothetical for valsartan and two in
13 your hypothetical for Taxotere, correct?

14 A. Yep.

15 Q. The next sentence is
16 "Suppose that we claim that there is a
17 statistical significant difference
18 between these two groups when the P-value
19 of any one of these three trials is less
20 than .05."

21 In Taxotere you put "Suppose
22 that we claim there is a significant
23 difference between these two groups
24 P-value of any of these two trials is

1 less than .05."

2 Almost identical except for
3 you use three in -- three trials in
4 valsartan and you used two trials in
5 Taxotere, correct?

6 A. Yeah. Because Taxotere only
7 has two clinical trials available at that
8 time.

9 Q. I see.

10 Next you put, "If we apply
11 this decision rule, the total Type I
12 error rate would be 14.3 percent. That
13 is, even if there were no differences
14 between the exposure and control with
15 respect to cancer incidence, the chance
16 of claiming either the exposed or control
17 is harmful is more than 14.3 percent."

18 In Taxotere you put, "If we
19 apply this decision rule, the total
20 Type I error rate would be 9.75 percent.
21 That is, even if there were no
22 differences between Taxotere and control
23 with respect to alopecia events, the
24 chance of claiming either Taxotere or

1 control is harmful is more than
2 "9.75 percent in at least one study."

3 Correct?

4 A. Yep.

5 Q. Those sentences are fairly
6 similar, except for in valsartan you're
7 looking at the hypothetical of three
8 trials, and in Taxotere you're looking at
9 the hypothetical of two trials, correct?

10 A. Yep.

11 Q. Interesting that you use the
12 same word "trials" for both valsartan and
13 Taxotere when valsartan doesn't have any
14 clinical trials.

15 Why did you use the word
16 "trial" there?

17 A. A trial and the study, I use
18 interchangeable.

19 Q. I see.

20 So in a observation study
21 you would call those trials?

22 A. Well, it depend on your
23 definition of a trial, right. If it a
24 trial, if it's a experimental study

1 prospective, and observational, we don't
2 call it observational trial, we call it
3 observational study.

4 Q. Well, there are no
5 experimental study prospectives in --
6 strike that.

7 Next is, "This problem is
8 compounded if we apply the same rule to a
9 large number of studies."

10 And in Taxotere, you put the
11 same statement, exact same statement,
12 "This problem is compounded if we apply
13 the same rule to a large number of
14 studies," correct?

15 A. Yep.

16 Q. And next you put,
17 "Therefore, when we analyze multiple
18 studies and statistical tests
19 simultaneously, any conclusion of
20 toxicity must be carefully interpreted
21 due to the multiplicity of tests."

22 On the other side you put,
23 "Therefore, when we analyze multiple
24 studies simultaneously, any conclusion of

1 toxicity has to be carefully
2 interpreted."

3 Those are similar sentences,
4 correct?

5 A. Yeah. I like to point out,
6 you see the words I use, "carefully
7 interpreted," right.

8 I didn't say you have to do
9 Bonferroni or not.

10 I just say, you have to be
11 carefully interpreted.

12 Q. Okay.

13 MR. MERRELL: Counsel, I
14 just wanted to talk about lunch.
15 We're getting sort of close to the
16 lunch hour. I don't know what you
17 have, if you're moving to
18 something else or what times makes
19 sense.

20 MR. NIGH: I think right now
21 is a good time to take a break.
22 How long do you guys want for
23 lunch?

24 THE VIDEOGRAPHER: The time

1 right now is 12:20 p.m. We are
2 off the record.

3 - - -

4 (Whereupon, a luncheon
5 recess was taken.)

6 - - -

7 THE VIDEOGRAPHER: The time
8 right now is 1:17 p.m. We're back
9 on the record.

10 MR. NIGH: Okay. Let's pull
11 up LP-1562, your Celebrex report.
12 And let's put that side by side
13 with your valsartan report.

14 BY MR. NIGH:

15 Q. We'll do similar what we did
16 with Taxotere.

17 First, though, in Celebrex,
18 Dr. Madigan wasn't on the opposite side
19 of you in Celebrex, correct?

20 A. Honestly, I don't remember.
21 Sorry.

22 Q. Do you remember who was on
23 the opposite side of you on Celebrex?

24 A. If I read in my report, I

1 can refresh my memory. Right now I'm not
2 quite sure.

3 Q. Does Dr. Milton Packer give
4 you an indication? Does that sound
5 familiar?

6 A. Milton Packer is our side,
7 is not opposite side.

8 Q. Oh, he's on your side.
9 Okay.

10 A. Yeah.

11 Q. But you don't recall who was
12 on the opposite side of you in Celebrex,
13 correct?

14 A. I think probably Dr. Nick
15 Jewel was one of those guys.

16 Q. Who did you say?

17 A. Nick Jewel out of Berkeley.
18 University of California, in Berkeley
19 campus. J-E-W-E-L.

20 Q. Okay. But you don't recall
21 Dr. Madigan being on the opposite side of
22 you in Celebrex, correct?

23 A. I vaguely remember he was.
24 But, you know, I'm not quite sure.

1 Q. Okay. Let's take a look at
2 your report side by side with Celebrex.

3 Now, in Celebrex, you were
4 also -- just like in Taxotere and for
5 valsartan, you were also retained by the
6 defendants who were pharmaceutical
7 companies in each -- in Celebrex as well,
8 correct?

9 A. Yes.

10 Q. Okay. Looking at the
11 screen, remember we talked about the
12 Celebrex report, we can pull that up so
13 we can quickly see it here. We looked at
14 this earlier today.

15 Do you recall that?

16 A. Yes, sir.

17 Q. Okay. Celebrex report,
18 that's dated March 30th, 2007. So that's
19 over 14 years ago, 14 and a half years
20 ago, correct?

21 A. Yeah.

22 Q. Okay. Let's go to paragraph
23 17 in valsartan. Let's look at Paragraph
24 8 in Celebrex. We'll do what we did

1 before, look at the side-by-side
2 comparisons.

3 Okay. Valsartan says,
4 "Suppose that we were interested in a
5 rate of occurrence" -- "Suppose that we
6 were interested in the rate of occurrence
7 of a certain clinical event, for example
8 cancer, among subjects exposed to NDMA or
9 NDEA to their counterparts (control)."

10 Next number for Celebrex, 14
11 and a half years ago, you put, "Suppose
12 that we are interested in the incidence
13 rate of a certain clinical event, for
14 example CV events, among patients treated
15 with Celebrex relative to the
16 corresponding rate for patients who have
17 been exposed to the drug."

18 Those are similar
19 sentences, correct?

20 A. Yeah. I believe this is
21 using the same statistical principle,
22 right, dealing with a similar case.

23 Q. Sure. The next sentence
24 says, "In the first step we take a sample

1 from a population of subjects exposed and
2 another sample from the population of
3 subjects who were not exposed."

4 Your next sentence in
5 Celebrex says, "To do this, we take a
6 sample from a population of patients
7 treated with Celebrex and another sample
8 from the population of patients who did
9 not receive Celebrex."

10 Similar sentences, correct?

11 A. You know, by changing a
12 word, right. You're in the first step
13 now, right.

14 Q. I recognize you changed a
15 word.

16 The next sentence says,
17 "Assuming that these samples are valid
18 representatives of the two populations,
19 quantitative analytic methods can be used
20 to determine whether the exposed group
21 has higher, lower, or similar event rate
22 than for the control group."

23

24

1 Your sentence in Celebrex
2 starts off the same way, "Assuming that
3 these samples are representative of the
4 two populations, statistical methods can
5 be used to determine whether the Celebrex
6 group has a different rate of CV events
7 than the non-Celebrex group."

8 Those are similar sentences,
9 correct?

10 A. Yes.

11 Q. Next, it says, "Since we
12 draw conclusions based on a subset of
13 subjects, any qualitative or quantitative
14 interpretation of the result, i.e.,
15 whether the rate is higher or not, is
16 subject to sampling error."

17 On the other one, you say,
18 "Since we draw conclusions based on a
19 subset of patients only, the" -- "any
20 qualitative or quantitative
21 interpretation of the result, i.e.,
22 whether the rate is higher or not, is
23 subject to so-called sampling error."

24 Very similar sentences,

1 correct?

2 A. Yes, sir.

3 Q. In valsartan, you put, "That
4 is, the observed event rate may be higher
5 leading to a false" -- "a possible false
6 positive finding, or lower, leading to a
7 possible false negative finding, than the
8 true event rate in the population."

9 In Celebrex, you say, "In
10 other words, the observed incidence rate
11 may be higher, leading to a possible
12 false positive finding, or lower, leading
13 to a possible false negative finding,
14 than the true incidence rate in the
15 population."

16 Very similar sentences in
17 the two expert reports, correct?

18 A. Yes, sir.

19 Q. Next you say, in valsartan,
20 "An efficient statistical method for
21 analyzing such data minimizes the chance
22 of making these two types of error."

23 In your Celebrex report, 14
24 and a half years ago, you say, "An

1 efficient statistical method for
2 analyzing such data minimizes the chance
3 of making these two types of errors."

4 Exact sentence in both of
5 those, correct?

6 A. Is that wonderful? Because
7 my principle is the same, right, for
8 14 years.

9 Q. I understand. Exact
10 sentence in both of those reports,
11 correct?

12 A. What's wrong with that, sir?
13 I don't understand your point. You can
14 go on for whole day to compare the notes.
15 I'm not quite sure where we're going from
16 here.

17 Q. Do you understand my
18 question?

19 A. I understand your question
20 perfectly. But I'm trying to say that
21 the principle of statistical methods are
22 valid. 20 years ago, today, they are the
23 same old thing.

24 Q. I understand what you're --

1 what you're saying. That's not my
2 question.

3 A. Could I finish? Could I
4 finish, please?

5 Q. Sure.

6 A. Can I explain that? Is that
7 okay I finish?

8 Q. My question is, are those
9 exact sentences in the two reports?
10 What's your answer?

11 A. I responded to you, I'm glad
12 that the same principle applied to
13 several cases.

14 Q. So is your answer, yes,
15 those are exact sentences in the two
16 reports?

17 A. Yeah, no problem. It's all
18 similar. They all the same. I don't
19 even understand why you repeat
20 everything, again, again, again.

21 Q. Next sentence, "It is
22 important to know that, except for the
23 exposure to NDMA or NDEA, the exposed
24 subjects in the sample should be similar

1 to the subjects in the non-exposed sample
2 with respect to important observable or
3 unobservable confounders."

4 In Celebrex, "It is
5 important to know that, except for the
6 usage of Celebrex, ideally the Celebrex
7 users in the sample should be similar to
8 the patients in the non-Celebrex sample
9 with respect to important observable or
10 unobservable confounders."

11 Gives two examples.

12 Those are very similar
13 sentences again, correct?

14 A. Yep.

15 Q. Looking at the next --
16 Number 18. And looking at Paragraph
17 Number 9. Looking at the next paragraph
18 in valsartan and the next paragraph in
19 Celebrex.

20 It says, "After we have
21 determined how to draw" -- in valsartan,
22 "After we have determined how to draw a
23 valid sample from the population of
24 interest, one has to determine what

1 clinical endpoints are most appropriate
2 to quantify the exposure effect."

3 In Celebrex, "Once an
4 investigator has determined the patient
5 population of interest, he or she must
6 draw a valid sample from the population."

7 Similar sentence, correct?

8 A. Yep.

9 Q. Then you go down to,
10 "Suppose that based" -- in valsartan.
11 "Suppose that, based on the sample of 100
12 patients at the end of the study, four
13 patients experienced such events."

14 In Celebrex, "Suppose that
15 based on the sample of 100 patients, four
16 patients experienced similar" --
17 "experienced CV events."

18 Similar statement, correct?

19 A. Well, one is for a CV event.
20 The other one is cancer, isn't it? Are
21 they different?

22 Q. They are very similar,
23 aren't they?

24 A. Well, how do you define

1 similar. I said this one case is for CV
2 event. The right-hand side is for cancer
3 incidence.

4 Q. You don't think that when it
5 starts out -- the sentence says, "Suppose
6 that, based on a sample of 100 patients,"
7 and the other one says, "Suppose that,
8 based on the sample of 100 patients," and
9 that for both hypotheticals, you assumed
10 four patients that experienced an event,
11 that those are similar sentences?

12 A. Well, whatever you say.
13 It's similar. But I'm saying address
14 different legal cases, right.

15 Q. Next sentence, "An obvious
16 estimate of the event rate for the
17 underlying population is .04 or
18 4 percent."

19 In Celebrex, "An obvious
20 estimate of the incident rate of toxicity
21 for the underlying population is .04, or
22 4 percent."

23 Those are very similar
24 sentences, correct?

1 A. Yep.

2 Q. Next sentence, "This is
3 called a point estimate."

4 In Celebrex, exact sentence,
5 "This is called a point estimate."
6 Correct?

7 A. Yep.

8 Q. Next sentence in valsartan,
9 "However, this estimate is based on a
10 sample of patients."

11 Celebrex, "However, this
12 answer" -- "this estimate is based on a
13 relatively small set of patients."

14 Similar sentence, correct?

15 A. Yep.

16 Q. Next sentence, "The true
17 event rate for the entire population may
18 be more or less than 4 percent."

19 Next sentence in Celebrex,
20 the true incidence rate for the entire
21 population may be more or less than .04."

22 Very similar sentence,
23 correct?

24 A. Yep.

1 Q. Next sentence, "Different
2 studies generating different samples may
3 find a different" -- "may find different
4 proportion of subjects with cancer."

5 Next sentence, "Another
6 investigator using a different sample or
7 study may find that none of the patients
8 experienced a CV event."

9 The following sentence,
10 "Therefore, when observing results from a
11 single sample, it is important to attach
12 a level of confidence to the observed
13 point estimate."

14 In Celebrex, 14 and a half
15 years ago, you put, "Therefore, when
16 observing results from a single sample,
17 it is important to attach a level of
18 confidence to the observed point
19 estimate."

20 Those are the exact same
21 sentence, correct?

22 A. Yeah. I'm glad I am
23 consistent.

24 Q. Looking at valsartan, "This

1 quantitative scientific process is called
2 drawing or making inferences about the
3 true event rate."

4 In Celebrex, "This
5 quantitative scientific process is called
6 drawing inferences about the true
7 incident rate."

8 Very similar sentences,
9 correct?

10 A. Yep.

11 MR. NIGH: Turning to Number
12 19, and Paragraph 15 in Celebrex.

13 BY MR. NIGH:

14 Q. In valsartan, you start out,
15 "Let me turn to the issues of comparing
16 two groups of subjects, one having been
17 exposed and the other being in the
18 control."

19 In Celebrex, 14 and a half
20 years ago, you say, "Let me turn to the
21 issues of comparing two groups of
22 patients, one receiving Celebrex and the
23 other receiving a placebo."

24 Very similar sentences,

1 correct?

2 A. Mm-hmm. Yes.

3 Q. The next sentence, "To make
4 sure the two samples of subjects are
5 comparable with respect to all potential
6 confounders, we often rely on a
7 randomized clinical trial setting."

8 In Celebrex, "To make sure
9 the two samples of patients, example
10 Celebrex and placebo, are comparable with
11 respect to all potential confounders,
12 investigators often rely on a randomized
13 clinical trial setting."

14 Very similar sentences,
15 correct?

16 A. Yep.

17 Q. In valsartan, you say, "Such
18 a clinical study yields a well designed
19 experiment that has the potential for
20 generating reliable prospective data on
21 safety."

22 In Celebrex, you say, "Such
23 a medical study yields a well designed
24 experiment for generating reliable

1 prospective data on drug efficacy or
2 safety."

3 Very similar sentences
4 again, correct?

5 A. Yep.

6 Q. And in valsartan, you say,
7 "Such studies were conducted and
8 monitored according to a pre-specified
9 protocol, which details the exposure
10 administered (for example, form, dosage
11 frequency), the clinical or biological
12 endpoints (example, lab value, patient's
13 quality of life, time to remission, time
14 to toxicity event), the study patient
15 population, and other clinical and
16 statistical considerations."

17 In Celebrex, you say, "Such
18 studies are conducted and monitored
19 according to a pre-specified protocol
20 which details the treatments administered
21 (example, form, dosage, frequency), the
22 clinical or biological endpoints (for
23 example, lab value, patient's quality of
24 life, time to remission, time to a

1 toxicity event), the study patient
2 population (elderly, suffering from
3 rheumatoid arthritis), and other clinical
4 and statistical considerations."

5 Those sentences are very
6 similar, correct?

7 A. No. It's quite different in
8 my opinion, right. I said elderly,
9 something like that.

10 Do I have that on the
11 left-hand side?

12 Q. Yeah. You don't think those
13 sentences are very similar, it's almost
14 identical, except for Celebrex you say
15 "elderly and suffering from rheumatoid
16 arthritis."

17 A. Well, if you want to say
18 similar, that's fine with me. I said a
19 while -- I always aim it at a specific
20 legal case, right. I'm modifying my
21 words -- the words I use before, I'm so
22 glad and still confident that 14 years
23 ago I used it, still applicable today,
24 right. That's a good thing, right?

1 Staying with a --

2 Q. It's a good thing for
3 pharmaceutical companies that they have a
4 cookie-cutter report and know what your
5 opinion is going to be before they hire
6 you, correct?

7 MR. MERRELL: Objection to
8 form. Argumentative.

9 THE WITNESS: Sir, that's
10 not fair to say -- safe to say.

11 BY MR. NIGH:

12 Q. Okay. Let's take a look at
13 the next sentence. "The trial is usually
14 randomized and blinded."

15 Do you see that?

16 A. Yep.

17 Q. And in Celebrex, it says,
18 "The trial is usually randomized and
19 blind."

20 Very similar sentences,
21 correct?

22 A. Yep.

23 Q. Next in valsartan, it says,
24 "Subjects are assigned randomly to one of

1 the study arms and neither physicians nor
2 patients are told whether the patient is
3 receiving an active exposure or a
4 control."

5 In Celebrex, 14 and a half
6 years ago, you put, "Patients are
7 assigned randomly to one of the study
8 arms and neither physicians nor patients
9 are told whether the patient is receiving
10 an active drug, Celebrex, or a placebo."

11 Very similar sentences,
12 correct?

13 A. No. To me, they're quite
14 different.

15 Q. Okay. The wording is almost
16 in the exact same order in both
17 sentences. All you've done is subbed out
18 what's relevant to Celebrex versus
19 valsartan, right?

20 A. To me it's quite different,
21 isn't it?

22 Q. Okay. Well, we'll let the
23 jury look at that and decide.

24 The next sentence says,

1 "This avoids selection bias or other
2 experimental bias."

3 In your other report you
4 say, "This avoids selection bias or other
5 experimental bias."

6 The exact same sentence,
7 correct?

8 A. Yep.

9 Q. Next, you say, "When
10 appropriately designed, results from a
11 well conducted randomized clinical trial
12 are regarded as a gold standard in
13 controlled settings to evaluate the
14 efficacy and safety of an exposure."

15 In Celebrex, you say,
16 "Results from a well conducted randomized
17 clinical trial are regarded as a gold
18 standard in controlled settings to
19 evaluate the efficacy and safety of a
20 treatment."

21 Very similar sentences,
22 correct?

23 A. Yep.

24 Q. And again, in valsartan, we

1 don't have any clinical trials assessing
2 increased risk or whether there's an
3 increased risk with contaminated
4 valsartan, correct?

5 A. I just point out what is the
6 gold standard for evaluating an exposure.
7 That's what I'm trying to say. I didn't
8 say anything about valsartan case. But
9 yeah, if you read the -- go on and read
10 my next paragraph, you can see it, right.

11 You can see there's a gold
12 standard. Unfortunately, we cannot do
13 it. As you said very well this morning,
14 we cannot randomize the patient, right.

15 Q. Right.

16 MR. NIGH: Looking at --
17 looking at Page 19, Paragraph 31,
18 and look at Paragraph 14 in
19 Celebrex.

20 31, please. Those are the
21 references. Paragraph 14.
22 Further up.

23 BY MR. NIGH:

24 Q. In valsartan, you start off

1 with, "Even if we accept Dr. Madigan's
2 criteria that the false positive rate of
3 .05 is an arbitrary threshold value, this
4 procedure was generally used to establish
5 the so-called statistical significance of
6 a report when testing a single clinical
7 endpoint in a single study."

8 In Celebrex, you put, "The
9 95 percent level for the confidence
10 interval or the 5 percent level of
11 significance for testing hypothesis is
12 typically used by investigators and
13 statisticians to establish the
14 statistical significance of a result when
15 testing a single clinical primary
16 endpoint."

17 Similar ideas quoted in each
18 of these, correct?

19 A. No, I don't think it's
20 similar. But it is the same principle.

21 Q. Well, let's look at the next
22 sentence.

23 You put, "This level can be
24 very liberal."

1 And on the other side, you
2 put, "This level can be very liberal."

3 That's identical thus far,
4 right?

5 A. Yep.

6 Q. And next in valsartan, you
7 wrote, "I.e., can result in statements of
8 statistical significance when none
9 exists."

10 In Celebrex, 14 and a half
11 years ago, you put, "I.e., can result in
12 statements of statistical significance
13 when none exist."

14 Those are identical,
15 correct?

16 A. I'm glad it's still 14 years
17 after, still valid argument.

18 Q. And in valsartan, you put,
19 "If multiple statistical tests and/or
20 studies are examined simultaneously."

21 In Celebrex, you put, "If
22 multiple endpoints are examined
23 simultaneously."

24 Very similar, correct?

1 A. Yeah.

2 Q. Looking next you've got,

3 "When using" -- using --

4 MR. NIGH: Going down,

5 "Using the 5 percent rule."

6 BY MR. NIGH:

7 Q. "Using the 5 percent rule
8 for claiming statistical significance to
9 analyze simultaneously a large number of
10 tests in a study will yield a high rate
11 of false positive findings."

12 In Celebrex, "Using the 5
13 percent rule for claiming statistical
14 significance to analyze simultaneously a
15 large number of endpoints in a study will
16 yield a high rate of false positive
17 findings across all endpoints."

18 Very similar statements,
19 correct?

20 A. Yep.

21 Q. Next you put, "Often, the
22 overall false positive rate could be as
23 high as 20 percent or more, that is, a
24 very high chance of finding exposure is

1 not safe with respect to control, when in
2 fact there is no difference between the
3 two groups."

4 Your next sentence in
5 Celebrex, "It is not unusual that when
6 the 5 percent test hypothesis rule is
7 applied simultaneously to a number of
8 endpoints in the study, the overall false
9 positive rate is as high as 20 percent,
10 that is, a very high chance of claiming a
11 drug is not safe with respect to placebo
12 when in fact there is no difference
13 between the two groups."

14 Very similar statements,
15 correct?

16 A. Okay.

17 Q. Taking a look at 30 -- so
18 you've made the statement multiple times
19 that you're glad you're consistent
20 between your reports back in, you know,
21 14 and a half years ago.

22 Have you been consistent
23 with reports even longer and earlier than
24 that?

1 A. Well, if you can show me,
2 I'd be happy to read it.

3 Q. You don't know? Do you --
4 were you continuing to use these
5 cookie -- a lot of these same
6 cookie-cutter statements in reports that
7 you did before Celebrex 14 and a half
8 years ago?

9 MR. MERRELL: Objection to
10 form.

11 THE WITNESS: You're asking
12 me if I did something earlier than
13 Celebrex study? That's what your
14 question, sir?

15 BY MR. NIGH:

16 Q. Yes.

17 A. I don't remember, sir.

18 Q. Now, you said earlier that
19 you don't hold yourself out to be a
20 toxicologist, correct?

21 A. Correct.

22 Q. And so you wouldn't consider
23 yourself to be an expert in toxicology,
24 correct?

1 A. Correct.

2 Q. You said earlier that you
3 don't hold yourself out to be an
4 epidemiologist, correct?

5 A. Correct.

6 Q. So you wouldn't consider
7 yourself to -- you wouldn't hold yourself
8 out -- or being -- sorry. Strike that.

9 So you wouldn't consider
10 yourself to be an expert in epidemiology,
11 correct?

12 A. Correct.

13 Q. You said earlier that you
14 don't hold yourself out to be a
15 pharmacologist, correct?

16 A. I remember -- I didn't
17 remember you asking me about it. But the
18 answer is no, I don't think I'm a
19 pharmacologist.

20 Q. So you wouldn't consider
21 yourself to be an expert in -- my
22 question was pharmacologist. Not
23 oncologist.

24 You wouldn't consider

1 yourself to be an expert at pharmacology,
2 correct?

3 A. That's correct.

4 Q. Okay. Now, Doctor, you said
5 that you analyzed two valsartan epi
6 studies, even though Dr. Madigan had not
7 looked at any valsartan epidemiology
8 studies, correct?

9 A. Yes, sir.

10 Q. What was your purpose for
11 looking at those two valsartan
12 epidemiology studies?

13 A. Well, you know, when I read
14 Dr. Madigan's report, he used dietary
15 studies, he used occupational study, to
16 infer the safety issue about an impurity
17 in valsartan.

18 I ask myself right away, how
19 come Dr. Madigan did not use a direct
20 route and to understand the safety issue
21 of impurity in valsartan.

22 So I believe -- forgive me,
23 I don't know the sequence. Either I ask
24 the lawyers or the lawyer actually

1 already send the papers to me, which is
2 two studies. One is being called a
3 Danish study, the other one we call the
4 German study.

5 And I read both. I say,
6 wow, those directly addressed issue about
7 impurity questions, which are more
8 relevant to our question in this legal
9 case, compared with the way Dr. Madigan
10 approach.

11 That's why I think it's
12 important to point out there were studies
13 available directly addressed your
14 question. Period.

15 Q. What do you think the
16 purpose of Dr. Madigan's report -- expert
17 report was?

18 A. The purpose of Dr. Madigan,
19 of course, obviously, he want people to
20 extrapolate the results from dietary
21 studies or occupational study to
22 valsartan case. That's my understanding.

23 Q. What kind of results was he
24 trying to extrapolate, what were the

1 results referring to from the dietary
2 studies and the occupational exposure
3 studies?

4 A. We can go over Dr. Madigan's
5 report, you know, line by line and figure
6 out, okay, what he wants to do.

7 Q. No. I'll bring up the
8 report if we need to. But I'm asking
9 you, in terms of your knowledge, what
10 kind of -- the purpose or what kind --
11 strike that. I'll start over.

12 What kind of results was he
13 trying to extrapolate? What were the
14 results referring to from the dietary
15 studies and the occupational exposure
16 studies?

17 A. Can we actually go to his
18 report?

19 Q. This is a big picture
20 question. It's not a line-by-line
21 question.

22 A. What?

23 Q. I said this is a big picture
24 question. It's not a line-by-line

1 question.

2 What was the purpose of his
3 report in terms of extrapolating results?
4 What kind of results was he trying to
5 extrapolate?

6 A. Well, he did many things.
7 I'm not quite sure how I can use one
8 sentence to summarize for you.

9 I think the best way, if we
10 get both reports and we all can
11 understand what he wants us to understand
12 it, what my comments about it, right.
13 That's fair game.

14 Instead you're asking me,
15 what do you think about what Dr. Madigan
16 wants us to understand, right.

17 I mean, let's go through his
18 report. And I'm going to answer you what
19 he wants us to understand.

20 Q. Are you saying that without
21 looking at the report right now, you
22 can't answer the question as to what the
23 purpose of his report was in terms of
24 extrapolating results from dietary

1 studies and occupational exposure
2 studies?

3 A. Sir, he did so many things,
4 I cannot give you one sentence to
5 summarize what I got from his report.

6 And if you wanted to know
7 my -- the overall disagreement, you can
8 just go back to my executive summary.
9 Also, my conclusions, right. You can
10 understand exactly what my positions are
11 and what I have concerns about
12 Dr. Madigan's report.

13 I can read it for you, if
14 you wanted to. I can read my summary,
15 also my conclusion.

16 Q. I've read your report and
17 your summary and your conclusions many
18 times. Okay. I don't need to read that
19 word for word during this deposition.
20 I've done it many times. I don't need
21 the instruction on what to go to for your
22 opinions.

23 I'm asking a simple
24 question.

1 And the best that you can
2 answer it, what do you think he was
3 trying to extrapolate from the dietary
4 studies and occupational exposure
5 studies?

6 MR. MERRELL: Objection to
7 form. Asked and answered.

8 THE WITNESS: I cannot
9 answer you.

10 BY MR. NIGH:

11 Q. What was he looking at in
12 the dietary studies and the occupational
13 exposure studies? What sort of figures?

14 A. If you allow me to go
15 through his report, I can answer you. I
16 cannot answer you without looking at the
17 report, and my report.

18 Q. As you sit here right now,
19 you can't tell us, you know, what results
20 he was looking at, just in general, or
21 describe them in dietary and occupational
22 exposure studies?

23 A. Well, sir, listen, why don't
24 you just go to my -- let me use mine.

1 You don't have to read it. You said you
2 read my report word by word, okay.

3 I'm going to read what I
4 wrote, and I'll tell you what he
5 translate from dietary to valsartan case.
6 Is that okay?

7 Q. Sure.

8 A. Conclusion. Paragraph 37.

9 Right. Dr. Madigan claimed
10 that NDMA statistically significantly
11 increased gastric cancer risk arise in
12 LCEs as low as 1,962 ug, is the number.
13 The equivalent threshold for lung cancer
14 so-and-so, for the other cancer, and et
15 cetera, right? Blah, blah, blah, blah.

16 Based on the report by
17 Dr. Madigan, that's what you try to
18 convince us. He said well, listen, guys,
19 if you have this ratio of so-and-so, you
20 have high risk to get cancer, different
21 cancer. Right.

22 I'm saying those claims
23 cannot be justified with the issues and
24 the concerns I raise in this report.

1 That's 37, okay.

2 38, the same concerns apply
3 to the claims in Paragraph 34 in
4 Dr. Madigan's report. Dr. Madigan's 34,
5 that's the methods, he want to send to
6 us, right. That's -- answer your
7 question.

8 So moreover, those essential
9 values may not be transportable in the
10 case of impurity -- I shouldn't use
11 contaminated -- valsartan without
12 appropriate validation, okay.

13 But he wanted us to believe
14 the findings from dietary study or
15 occupation study can be transported
16 automatically to the valsartan case,
17 right, with those threshold numbers.

18 That's my understanding,
19 okay.

20 Q. You understand that at no
21 time in all of Dr. Madigan's report does
22 he ever use the word "threshold values"
23 in describing those values, correct?

24 A. I don't remember. But I

1 quote here "the equivalent threshold for
2 lung cancer" is so-and-so. If I
3 misquoted the word "threshold" I
4 apologize. Right.

5 Q. Back to my original
6 question. He was looking at -- what is
7 the LCE?

8 A. The way I understand,
9 lifetime exposure for the contaminant.

10 Q. And that would be lifetime
11 exposure of what?

12 A. From NDMA, for example.

13 Q. And what would the ug refer
14 to?

15 A. I'm sorry?

16 Q. What would the ug refer to
17 in his report? What was your
18 understanding of what that refers to?

19 A. AOGE, you're talking about?

20 Q. No, ug. You used the words
21 "ug" in your reading you're --

22 A. Oh, it's a measurement.
23 It's smaller than milligram, mg.

24 Q. What does -- what does ug

1 stand for?

2 A. I don't remember exactly. I
3 think it's smaller than mg. I don't know
4 what its scale, smaller than mg.

5 Q. You don't know ug refers to
6 or what he's referring to in this report,
7 when you put ug?

8 A. I can copy what Dr. Madigan
9 say.

10 Q. You just copied what
11 Dr. Madigan stated, but you don't know
12 what the ug means?

13 A. Ug is a scale which measure
14 how much the exposure, right, like a g,
15 mg, like ug. That's a different scale,
16 measure how much contamination in the
17 blood or whatever in your body.

18 Q. Explain quantitatively what
19 ug means?

20 A. I don't remember how to
21 define, sir.

22 Q. Do you know what ng means?

23 A. Mg?

24 Q. N. N as in Nancy. Ng, do

1 you know what ng means?

2 A. I don't know.

3 Q. Okay. Do you know what mcg
4 would refer to?

5 A. No. I'm not a toxicologist.
6 I don't know the scale.

7 Q. So when you see him put
8 4,000 -- or just -- sorry, the first one
9 that you have quoted in Number 37,
10 "Dr. Madigan claimed that for NDMA" --
11 actually let's do this. Let's put this
12 up on the screen.

13 MR. NIGH: LP -- so the jury
14 can see it too -- LP-1557.

15 This was previously marked
16 Exhibit 3.

17 And turn to number --
18 Paragraph 37. And let's blow that
19 up.

20 BY MR. NIGH:

21 Q. This is in your report.

22 MR. NIGH: Blow up Paragraph
23 37.

24

1 BY MR. NIGH:

2 Q. So in your report you put in
3 Paragraph Number 33 in the report,
4 "Dr. Madigan claimed that for NDMA
5 statistically significant increased
6 gastric cancer risk at LCEs as low as
7 1,962 ug."

8 What does that refer to
9 quantitatively, 1,962 ug?

10 A. I am not a toxicologist. I
11 cannot answer you how much is that
12 exposure.

13 Q. That doesn't take a
14 toxicology opinion to know what ug means,
15 right?

16 A. I don't know, sir.

17 Q. So you don't know what
18 Dr. Madigan was referring to when he put
19 the word ug or the letters ug, and you
20 couldn't tell this jury quantitatively
21 what he's referring to when he says 1,962
22 ug, right?

23 A. I don't know how much he's
24 mentioning to quantify this.

1 Q. Do you know how he
2 calculated these LCEs, what formula?

3 A. Well, he calculate -- sorry.
4 Sorry, sir. Say it again.

5 Q. Do you know how he
6 calculated these LCEs or what formula he
7 used?

8 A. Oh, yeah, yeah, I know
9 mathematic formula. So what he did is
10 following: He compared this Q1 to
11 quarter -- the lower dose, that exposure
12 against the Q4, which is the highest
13 dose.

14 Sometimes he use five set
15 instead of four. And then he compared
16 the Q1 against the Q4. Then if he says
17 it's statistically significant, then I'm
18 going to take this study, the exposure
19 level, whichever he described, that's
20 Study Number 1, right.

21 Then we go to another study.
22 If it's not a statistically significant,
23 he dropped it.

24 Then he go to the third

1 study. If he find a statistical
2 significant, he count -- he take the
3 highest, the Q4, the level, right, for
4 the lifetime exposure, which I don't know
5 how much to quantify. That's what he
6 explains.

7 And then he added up, take
8 an average. That's my understanding, he
9 calculated the so-called lifetime
10 threshold value.

11 Q. Have you ever calculated
12 lifetime cumulative exposures in any of
13 the work that you've done?

14 A. No.

15 Q. So this is -- this is novel
16 to you, when you see these calculations
17 of lifetime cumulative exposures,
18 correct?

19 A. Novel in a way. Is not a
20 statistical novelty because statistical
21 is very straightforward. That's what I'm
22 concerning about his statistical argument
23 and the claim.

24 I cannot interpret the

1 physical meaning of this exposure, the
2 level we're talking about.

3 Q. I'm not sure you understood
4 what he was doing, because you just
5 mentioned that if he found that it wasn't
6 statistically significant, he would drop
7 it.

8 Why do you think that?

9 A. Well, that's my
10 understanding. If I misunderstood what
11 he did, I apologize.

12 Q. He has Table 1, and he's
13 calculated LCEs for nearly every single
14 dietary study. Did you realize that?

15 A. Hold on a second. Let me
16 see the Table 1 here. Okay.

17 MR. NIGH: Yeah. Let's go
18 ahead and show it. LP-1558.

19 Table 1.

20 BY MR. NIGH:

21 Q. It's important if you're
22 going to criticize an expert's opinion,
23 that you understand what they're doing,
24 correct?

1 A. Oh, absolutely.

2 Q. Okay. Looking at Table 1,
3 do you see here how he calculated LCE for
4 nearly every single dietary study?

5 A. Yeah, he lists the LCE and
6 every study they have -- well, some is
7 missing. But okay, yes.

8 Q. Nearly every one. He
9 doesn't have one for Knekt.

10 Do you see that?

11 A. Yeah.

12 Q. Do you know why he wouldn't
13 have one for Knekt?

14 A. No, sir.

15 Q. Do you know if Knekt gave
16 the value of NDMA in the fourth quartile?

17 A. I'm sorry, sir. I don't
18 understand your question.

19 Q. Now, looking at this, can
20 you explain -- let's just take a look at
21 Palli. And you see under LCE, it shows
22 5,260?

23 Do you see that?

24 A. Yes, sir.

1 Q. And that's one -- that's SS.
2 What do you think SS stood for?

3 A. The effect size, you're
4 talking about.

5 Q. You think SS on his chart
6 stood for sample size?

7 A. You mean the last two -- the
8 column statistical significance? Is that
9 what you're talking about? Or which one
10 are you talking about?

11 Q. SS?

12 MR. NIGH: Can we highlight
13 that column.

14 BY MR. NIGH:

15 Q. What do you believe that
16 stood for, that SS?

17 A. I don't know, the SS means.

18 Q. Okay. Did you happen to
19 pull these dietary studies to where you
20 could figure out what the SS meant in his
21 table?

22 A. No, sir.

23 Q. What do you think effect
24 size meant?

1 A. Effect size, if I interpret
2 it correctly, that's the one we are
3 talking about in the morning, about for
4 example the difference between the two,
5 you can use the hazard ratio, you can use
6 odds ratio, you can use risk ratio, et
7 cetera.

8 Q. Right. Odds ratio, risk
9 ratio and HRs, are are all commonly
10 referred to as effect, or effect size,
11 correct?

12 A. Yes, sir.

13 Q. Okay. But you don't know
14 what the SS, right next to that stands
15 for in the table?

16 A. I -- I don't know. I better
17 not make a guess. But I think I know
18 what is going on. But I apologize. I
19 don't want to say -- I'm not 100 percent
20 sure. I don't want to say anything.

21 Q. Well, you're commenting on
22 his report. That's what you were hired
23 to do, correct?

24 A. Yes, sir.

1 Q. So I'm asking you, what do
2 you think his report, the SS stood for?

3 A. I don't know.

4 Q. Okay. Next, do you remember
5 you asked about country, that second
6 column on this table. You raised
7 country. Doesn't he provide the
8 countries here?

9 A. Provide country to me?
10 Sorry.

11 Q. For each study. Doesn't he
12 provide the countries for each study?

13 A. In the table, yes.

14 Q. Right.

15 A. Yes, in the table.

16 Q. And design, what do you
17 think the CC or the C stands for?

18 A. Sorry. Where is the CC?
19 I'm sorry.

20 Q. Right underneath "Design."
21 Do you see CC and C?

22 A. Oh, I have no idea what CC
23 means.

24 Q. So as you reviewed his

1 expert report and this table, you didn't
2 know what CC stood for or what C stood
3 for?

4 A. Yeah, because that's not
5 relevant for statistical analysis.

6 Q. The type of study or the
7 design of the study can be relevant,
8 right?

9 A. Well, I don't know, what
10 kind of observational study or what,
11 because basically, he didn't tell us
12 exactly what's going on in the report.
13 Right. Did he say anything about CC
14 here. In the footnote, did he indicate
15 CC?

16 Q. Did you pull the studies to
17 see what CC or C may refer to?

18 A. No, because I am basically
19 using his report. Anything he send to
20 me, I would read it very carefully. But
21 if he skip it, I said well, that's your
22 problem. It's not my problem.

23 Q. But you don't understand
24 what he's referring to. And commenting

1 on his report, if you don't understand
2 it, isn't that your problem?

3 A. I don't think so. Because
4 he's got very important statistical
5 analysis, he would have put a footnote
6 underneath the table. Say what do you
7 mean by CC, what do you mean by SS.

8 Q. Why do you think -- what
9 makes you think he's required to do that?

10 A. Otherwise, how in the world
11 the people outside the field understand
12 what he's talking about.

13 Q. Show studies. Just pull up
14 the studies, right.

15 A. All right. How in the world
16 would you --

17 Q. Just pull up the studies to
18 see what it stands for.

19 A. You talk over me. If
20 that -- if you want to talk, I'll let you
21 talk first.

22 I just want to share with
23 you, you're asking me how come I don't
24 ask Dr. Madigan what CC means. I say

1 well, listen, he didn't even list it,
2 right. He didn't explain to me in the
3 report.

4 And I was told my assignment
5 is to look at the report. I don't have
6 to question about Dr. Madigan did. I say
7 well, listen, if you give me the
8 information, I use it. If you don't give
9 me information, I don't use it.

10 Q. Well, he gives you the
11 information because he cites to every one
12 of these studies. So you can simply --

13 A. But what --

14 Q. Hold on. I was asking the
15 question that time.

16 A. Yeah.

17 Q. So you can pull up the study
18 to see what the design of that study is
19 and figure out what his CCs and Cs are
20 referring to on this chart, right?

21 A. Nope. I can't.

22 Q. You don't think you can?

23 A. Sorry?

24 Q. You don't think you can do

1 that?

2 A. He should have for us. Why
3 should we go into each study to check
4 what he mean by CC, what is a single C,
5 what is a double C?

6 Q. Okay. So you don't have any
7 criticism in terms of the designs of
8 these studies or how we look at design of
9 study in terms of extrapolating these
10 results?

11 A. I don't have information
12 about his abbreviation. Say -- this
13 study he gave a double C, the other one
14 is a single C.

15 But for most of studies, I
16 go into the study to understand what kind
17 of observational study they conducted.
18 Is it prospective or actually
19 retrospective? Is it cohort study or
20 meta-analysis?

21 That's what I did. I don't
22 have to go in to ask Dr. Madigan what
23 he's talking about, what is a CC, or what
24 does a C means.

1 Q. Okay. Next column, base
2 high dose ug.

3 What does that refer to?

4 A. That's, my understanding Q4,
5 whatever you want, base on high value.

6 Q. Okay. Your understanding is
7 that would be the highest quartile?

8 A. Well, sometimes use
9 different topic, right, not only the
10 quartile, something else.

11 Q. Okay. How about average --
12 approximate average age. What does that
13 refer to?

14 A. That's probably obvious,
15 right. That's -- everybody understands
16 average age. That's the study
17 population, I believe.

18 Q. You believe that's the
19 average age in the study?

20 A. Of the subjects.

21 Q. Okay. Explain that to me
22 more. You believe that's the average of
23 all the subjects in the study?

24 A. Well, I better check the

1 papers. And I can confirm you the 60 is
2 exposure time of the age of exposure, or
3 the age of the subject, right, in the
4 study, right.

5 Q. Okay. But as you sit here
6 right now, looking at this table from his
7 chart, you couldn't tell me one way or
8 the other?

9 A. Yeah. I need to
10 double-check.

11 Q. Okay. Looking at LCE ug,
12 what does that mean?

13 A. Well, as I explained before,
14 he took large -- the highest dose, right
15 tried to figure out the actual level,
16 LCE. That's how he figure out lifetime
17 exposure.

18 Q. Okay. So explain to me what
19 you think his formula was in looking at
20 this table to come to 5,260 for Palli,
21 LCE?

22 A. Well, this is -- my
23 understanding is he just copied from the
24 paper. He didn't do himself. He doesn't

1 have the data. He doesn't have the data
2 for patient, right.

3 Q. You think he copied the
4 5,260 LCE from the Palli study?

5 A. I believe that's my
6 understanding.

7 Q. Do you think that all of
8 these numbers under LCE --

9 MR. NIGH: Let's highlight
10 all of those in yellow, all the
11 way down.

12 THE WITNESS: Well, that's
13 what my understanding.

14 Otherwise, he should explain
15 to us how they calculate this
16 number, right.

17 With the individual patient
18 levels he calculated number, or
19 actually is it from the papers,
20 right.

21 He didn't explain too well.
22 He just give us a formula. Say,
23 well, that's calculated lifetime
24 exposure.

1 We said, do you have
2 individuals patient level?
3 Obviously, he didn't have it.
4 Right.

5 So those patients falling
6 into the Q4, for example, right,
7 he did not have those --
8 everybody's exposure level, right.

9 Okay. So I doubt he can
10 actually calculate this number
11 using individual patient level.

12 BY MR. NIGH:

13 Q. So is it your testimony that
14 you believe these numbers under LCE are
15 lifted from the papers?

16 A. I believe he find out from
17 the papers. Otherwise I'm not quite sure
18 how he calculated those numbers.

19 Q. But as you sit here right
20 now, looking at this table, which is a
21 table in Dr. Madigan's report -- it takes
22 up the full page in his report -- you
23 don't know whether or not those LCE
24 values were lifted directly from the

1 studies?

2 A. You're asking me if those
3 numbers are from the papers, right?
4 That's what you are asking, right?

5 Q. My question was, as you sit
6 here right now, looking at this table,
7 which is a table in Dr. Madigan's report,
8 it takes up the full page in his report.
9 You don't know whether or not those LCE
10 values were lifted directly from the
11 studies, correct?

12 A. I'm saying he cannot
13 calculate this number using individual
14 patient-level exposure.

15 Q. So do you know if they were
16 lifted directly from the studies or not?

17 A. It must be somewhere.
18 Summary statistics from the paper.
19 Otherwise I don't know how he calculate
20 it.

21 MR. NIGH: Okay. Let's go
22 ahead and take this down.

23 BY MR. NIGH:

24 Q. Okay. Back to my questions

1 earlier on -- Dr. Madigan's purpose was
2 to look at the cumulative exposure to
3 NDMA that led to increased risk of
4 cancers, correct?

5 A. Yes, sir.

6 Q. Now, the two valsartan
7 studies that you looked at, they don't
8 discuss how much exposure that the
9 patients had to NDMA? They don't
10 quantify exposure to NDMA in Pottegard or
11 Gomm, the amount of exposure to NDMA,
12 correct?

13 A. I have to read the paper
14 again. But my recollection, they did not
15 give a specific individual patient
16 exposure level. But again -- sorry.

17 Q. So --

18 A. But again, I needed --

19 Q. Go ahead.

20 A. Go back and read -- I'm
21 sorry.

22 I had to go back to read the
23 paper.

24 Q. So if Pottegard and Gomm

1 don't contain the amount of NDMA that
2 those patients -- that the patients were
3 exposed to in those studies, that would
4 not be useful to Madigan if his sole
5 purpose was to try to look at how much
6 NDMA it would take to lead to increased
7 risk of cancer, correct?

8 A. Well, again, sir, I don't
9 know in those two papers they have
10 individual exposure value or not. I
11 don't know. I have to read again.

12 Q. I started out with the
13 assumption that if Pottegard and Gomm do
14 not contain the amounts of NDMA that the
15 patients are exposed to -- so starting
16 with that hypothetical.

17 Follow me?

18 A. Sir, I not answer a
19 hypothetical question. I like to see the
20 fact.

21 Q. I'm allowed to ask you
22 questions as an expert that you take the
23 assumptions, okay.

24 So my first part that I want

1 you to assume that both Pottegard and
2 Gomm do not contain the amounts of NDMA
3 that its patients or subjects were
4 exposed to.

5 Do you follow me so far?

6 A. Yes, sir.

7 Q. If they do not contain the
8 amount of NDMA that they are exposed to,
9 then that would not be useful to
10 Dr. Madigan's question of how much NDMA
11 over a lifetime does it take to get
12 increased risk of cancer, correct?

13 MR. MERRELL: Objection to
14 form.

15 THE WITNESS: I'm not a
16 toxicologist, sir. I cannot
17 answer this question. I have no
18 opinion on this.

19 BY MR. NIGH:

20 Q. This isn't a toxicology
21 opinion.

22 The question is, you're
23 reviewing and you're responding to
24 Dr. Madigan's report. If those two

1 valsartan epi studies do not contain the
2 amount of NDMA that the subjects are
3 exposed to, then that would not be useful
4 to Dr. Madigan's question of how much
5 NDMA over a lifetime does it take to get
6 increased risk of cancer, correct?

7 MR. MERRELL: Objection to
8 form.

9 THE WITNESS: I don't answer
10 hypothetical question, even though
11 you have every right to ask me,
12 sir.

13 BY MR. NIGH:

14 Q. Are you refusing to answer
15 the question, in terms of assume
16 Pottegard and Gomm do not show how much
17 NDMA its subjects are exposed to?

18 A. I told you, sir, I have no
19 opinion on this.

20 Q. Okay. I'm going to ask this
21 again.

22 Assume that Pottegard and
23 Gomm do not show or discuss the amount of
24 NDMA that its subjects are exposed to.

1 If that's true, then those studies would
2 not be useful for Dr. Madigan in
3 calculating a cumulative amount of
4 exposure to NDMA that it takes to reach
5 increased risk of cancer, correct?

6 MR. MERRELL: Objection to
7 form. Asked and answered.

8 THE WITNESS: I have no
9 opinion, sir.

10 BY MR. NIGH:

11 Q. Do you have no opinion
12 because you believe that takes a
13 toxicology mindset to be able to answer
14 that question?

15 A. Probably.

16 Q. You believe that in order to
17 calculate a total amount of NDMA, that it
18 would be unuseful to try to use a study
19 that doesn't give you amounts of NDMA.
20 Is that your testimony?

21 A. Yeah, sir, the problem that
22 I am having here, is that before you even
23 talk about the lifetime exposure, pose
24 the argument without this lifetime

1 exposure for individual level, we have
2 trouble. We have a concerns about
3 Dr. Madigan's analysis, right.

4 You cannot even pass the
5 hurdle and say this exposed, this
6 unexposed. Do you have any causality or
7 association interpretation?

8 We couldn't even go through
9 that piece from the dietary studies or
10 occupational study. How in the world you
11 can go down the next level and claim
12 there was a threshold value, and beyond
13 that we have a concern for cancer risk?

14 So that's -- I said it very
15 clearly in my report. We couldn't even
16 go through the first hurdle to convince
17 us there was issue, even exposure to
18 unexposed impurity of valsartan. Right.

19 Then how we can actually go
20 to next level? That's my basic question
21 to Dr. Madigan, and also to you.

22 Q. My question, if you
23 understand his report, because the word
24 "threshold" doesn't show up anywhere in

1 his report, right?

2 A. I apologize if I use the
3 word "threshold." That's the number that
4 he used claiming, you know, beyond this
5 number we are in trouble, right. That's
6 my understanding, that's the common
7 language, right?

8 If I use the word
9 "threshold" improperly, I apologize. But
10 to me that's the same language we use all
11 the time to say what's the cutoff point,
12 what's cutoff value. We call that a
13 threshold value.

14 Q. He actually doesn't use the
15 word "cutoff" either.

16 A. Okay. That's fair. Which
17 language does he use then, sir?

18 Q. Do you understand that he's
19 not explaining a cutoff, a threshold,
20 line in the sand, none of those. He
21 doesn't use any of that language, right?

22 A. Okay. Yeah, so he may -- if
23 the level -- if the patient's exposure
24 level, beyond that number he quoted, that

1 means this guy have increased cancer
2 risk. Is that correct? That's what he
3 claimed, correct?

4 Q. Do you see that claim
5 anywhere?

6 A. Yeah, I mean, that's what he
7 is talking about in conclusion.

8 Q. Okay. Now, you talked about
9 causality.

10 As you read his report, did
11 you see a causation opinion that NDMA
12 causes cancer or that valsartan causes
13 cancer?

14 A. Well, sir, unfortunately he
15 said also very well in the deposition, he
16 was not in the position to talk about
17 causality at all. The most he can do is
18 talking about association.

19 Even association, we have
20 some question about it, right. And from
21 association to causality, none of those
22 arguments can be -- hold true, right. In
23 some sense we have no idea how to
24 interpret the causality now, right.

1 Q. Is it your testimony that
2 there is no association between NDMA and
3 cancer in humans?

4 A. Sir, I am not in a position
5 to tell you either way. I'm just
6 responding to my lawyers. My assignment
7 is asked very simple, do you think
8 Dr. Madigan's argument in his report is
9 valid? Okay. I'm saying his argument
10 has a lot of holes, and I don't agree
11 with his argument.

12 I didn't say either way it
13 was association, not association.

14 My point is that at this
15 point, we don't have much evidence to
16 claim either way. Because most
17 observational study, everybody has
18 limitation, okay.

19 So I'm not in the position
20 to tell you, sir, there's no association,
21 there is association. I just say we
22 don't have enough data to tell us either
23 way for valsartan case, not dietary, but
24 for valsartan case.

1 Q. My question to you is, is it
2 your testimony that there isn't enough
3 evidence to establish an association
4 between NDMA and cancers in humans?

5 MR. MERRELL: Objection to
6 form.

7 THE WITNESS: Correct. I
8 said there is not much evidence to
9 say there is association or there
10 is no association. That's my
11 position right now.

12 BY MR. NIGH:

13 Q. Now, you included Pottegard
14 and Gomm and looked at those studies.

15 Was that for you to form an
16 opinion on whether or not there's an
17 association between valsartan --
18 contaminated valsartan use and cancer?

19 A. Well, let me say this, sir.

20 I think the two studies are
21 pretty relevant to address the issue
22 regarding the impurity in valsartan.
23 Okay. It's very direct and to the point.
24 But everybody understands any observation

1 study has a limitation.

2 Those two studies had a
3 limitation, right.

4 So at this point, I said,
5 well, if I have a choice to look at
6 information about a valsartan impurity, I
7 would have put a more emphasis on these
8 two studies, instead of using a detour
9 method using dietary studies,
10 occupational study to tell me there is
11 some issue about a valsartan impurity.

12 So that's my position.

13 I'm not in the position to
14 say, yes, these two studies told us there
15 was no association about the cancer risk
16 and the impurity of the valsartan. And
17 I'm not in a position to say that either.

18 Q. Dr. Madigan was looking at
19 cumulative exposure and potential
20 increased risk from cumulative exposures
21 to NDMA.

22 How would you use Pottegard
23 or Gomm to assess cumulative exposures?

24 A. Well, sir, you asked me the

1 same question before. You said if they
2 didn't have -- under the hypothetical,
3 the assumption, there were no individual
4 exposure level using -- Dr. Madigan
5 cannot use their study or data to
6 calculate a so-called lifetime exposure.

7 I said I'm not in a position
8 to answer your question, because I would
9 really like to review that paper
10 carefully before I answer yours, right.

11 Q. Well, there's not even --
12 not just NDMA. But there's not even
13 enough data in terms of amount of
14 valsartan usage in Pottegard or Gomm to
15 try to draw any conclusions in the amount
16 of cumulative valsartan usage that it
17 would take to reach certain increased
18 risk in Pottegard or Gomm, correct?

19 A. Well, again, sir, forgive
20 me, I needed to read the paper carefully
21 again, because I've been -- I've not read
22 any their papers about -- after I
23 submitted the August 2nd report.

24 Q. So as you sit here right

1 now, you can't answer whether or not
2 there was enough information in Pottegard
3 or Gomm to draw any conclusions in the
4 amount of cumulative valsartan usage that
5 it would take to reach certain increased
6 risk in those studies, correct?

7 A. I don't recall, sir.

8 Q. Now, you included valsartan
9 epi to see whether these valsartan epi
10 studies, Pottegard and Gomm, demonstrate
11 the contaminated valsartan had an
12 association or not with cancer, correct?

13 A. Yes. We just simply stated
14 what -- the conclusion from the papers,
15 right. They didn't find association
16 between those two.

17 Q. Now, there are other -- you
18 understand that there are other drugs
19 that are -- also have been shown to have
20 NDMA, correct?

21 A. Well, I vaguely know a
22 little bit. Not much.

23 Q. Well, do you know that
24 losartan and irbesartan have been

1 demonstrated to have nitrosamines inside
2 of them?

3 A. I don't know, sir.

4 Q. Have you reviewed any
5 literature or epi studies to see whether
6 or not there was an association between
7 the nitrosamines in losartan or
8 irbesartan and increased cancer risk?

9 A. Well, if the reference are
10 not in Dr. Madigan's report, I don't
11 think I read it, except for those few
12 papers that I provide in my report.
13 Otherwise -- not an appendix -- Exhibit A
14 or B, if it's not in this, I didn't read
15 it.

16 Q. Right. Why wouldn't you
17 have looked at whether or not other
18 drugs that are contaminated with
19 nitrosamines had increased risk?

20 A. It was not in my assignment,
21 sir.

22 Q. But you looked at Pottegard
23 and Gomm, even though that wasn't cited
24 by Dr. Madigan, correct?

1 A. Well, you know, this is what
2 I said to you. I'm really curious how
3 come Dr. Madigan didn't use a direct
4 approach to actually use the valsartan
5 impurity study, right, to answer this
6 issue.

7 So I Googled. And it turns
8 out there were two, only two, that the
9 lawyers send to me, and I couldn't find
10 other studies available right now
11 directly address the issue.

12 So I thought, wow, gee, this
13 is interesting, how come Dr. Madigan did
14 not cite those two papers, right. To me,
15 that's all relevant to this particular
16 issue, the legal case.

17 Q. Well, you realize that it's
18 because they don't have any sort of
19 dosing to answer the question that he was
20 asked, right? No NDMA, no amount of
21 cumulative valsartan, right?

22 MR. MERRELL: Objection to
23 form.

24 THE WITNESS: Well, if I

1 were him, I would have mentioned
2 the papers about -- then you said
3 limitation of the two studies,
4 right. Instead he just totally
5 ignored and didn't even mention
6 anything in his report.

7 BY MR. NIGH:

8 Q. You realize there's four
9 other plaintiffs in this -- four other
10 plaintiff experts in this litigation, and
11 all the other four looked at valsartan
12 epi. But Madigan was only asked to look
13 at dose, right, you saw that from his --
14 from his -- the question that he was
15 asked, right?

16 A. Oh, no, sir. No, no, no,
17 no, sir. If you read Dr. Madigan's
18 report, first that he established this
19 so-called Q1 against Q4. And he cited
20 all the papers using the dosing-response
21 relationship. That's the first thing he
22 established.

23 You read this morning about
24 the lung cancer and other cancers, right.

1 That's what he did, first place.

2 Then he go in to figure out
3 this lifetime exposure level, right.

4 So we have two pieces. The
5 first piece, I have a serious concern
6 about his conclusion. If you cannot sort
7 out exposure, any exposure or a Q4, like
8 for example had some issues, how can we
9 actually go down the next level to figure
10 out what's the value your concerning go
11 about, right.

12 Q. Okay. So your questioning
13 is -- you know, your response to that is
14 he was also evaluating the strength of
15 association first?

16 A. Yeah. All the odds ratio
17 he's talking about -- he's compare the Q1
18 against Q4 or Q -- whatever he used,
19 quintile or quartile, whatever it is,
20 right, lowest against the highest dose,
21 whether there is statistical significance
22 or not. That's first step that he
23 established.

24 Q. Okay. Turning back to --

1 you realize there are other drugs that
2 have also been demonstrated to be
3 contaminated with NDMA, correct?

4 A. I don't know, sir.

5 Q. Are you aware that Zantac,
6 generic form name ranitidine, has been
7 demonstrated to be contaminated or have
8 NDMA?

9 A. I vaguely remember because I
10 was contacted by lawyers on the Zantac.
11 They actually -- I believe, either I
12 Googled or they send me some kind of
13 documents.

14 By the way, I was is not
15 retained for that case at all.

16 In any event, I notice
17 Zantac has impurity also.

18 Q. It's NDMA for Zantac,
19 correct?

20 A. Correct.

21 Q. And also metformin, some
22 metformin drugs have been contaminated or
23 have NDMA, correct?

24 A. That, I don't know.

1 Q. Did you review any
2 epidemiological studies for ranitidine
3 a/k/a Zantac, or metformin to see whether
4 they had increased risk of cancers?

5 A. No, sir.

6 Q. Why not?

7 A. Well, first, I was not
8 retained by the Zantac team, the legal
9 team, so I don't think I have the time to
10 even begin to understand the impurity of
11 other medicine.

12 Q. Well, you looked at studies
13 related to whether or not the NDMA in
14 valsartan, whether or not valsartan
15 showed increased risk of cancer. Why
16 wouldn't you look at other drugs that
17 also have NDMA and see if there's an
18 increased risk of cancer?

19 A. Well, because Dr. Madigan
20 didn't even mention about other
21 medicines, sir.

22 My job is mainly to address
23 an issue in Dr. Madigan's report.

24 Q. Dr. Madigan didn't look at

1 Pottegard or Gomm either, right?

2 A. Yeah. I don't know why.

3 And he didn't mention anything about
4 Zantac, metformin. I didn't see from his
5 report, unless I missed something.

6 Q. Did you think it wasn't
7 important to consider the other drugs or
8 other medications that had NDMA in
9 thinking about whether or not NDMA in
10 valsartan could cause increased risk?

11 A. Well, that's a very
12 interesting question. You should ask
13 Dr. Madigan how come he didn't include it
14 in his report, if you think such an
15 important issue. If you can actually
16 utilize to tally the evidence across all
17 the medicines, how come he didn't use it?

18 Q. Well, I'm asking you right
19 now.

20 Dr. Madigan --

21 A. Well --

22 Q. He didn't include Pottegard
23 or Gomm either.

24 A. Yeah.

1 Q. So I'm asking you.

2 A. Yeah, that's right.

3 Q. You included Pottegard and
4 Gomm.

5 A. Yeah.

6 Q. This question isn't for
7 Madigan. This isn't in relation to
8 Madigan. Let's throw Madigan out the
9 window right now. My question is to you.
10 You included Pottegard and Gomm?

11 A. Yeah.

12 Q. Okay. So you included those
13 two studies. Why else -- why didn't you
14 include the other studies that showed
15 NDMA in medications?

16 A. Sir, is this a case for the
17 valsartan impurity or is this a case for
18 Zantac impurity or metformin impurity
19 questions?

20 Is that -- I have to worry
21 about other medicine contamination to
22 answer your valsartan question?

23 You know, I have a problem
24 even to understand, you use a dietary

1 study, extrapolate a result to valsartan.
2 I said, you actually can use the
3 metformin result to this valsartan case?
4 The population is so different. The
5 patient population is so different,
6 right.

7 The Zantac population is
8 quite different than the valsartan
9 population.

10 So you are rounding a circle
11 here. You say, well, how in the world I
12 can use other treatment, other drug
13 contamination to help me? I said, well,
14 there's two studies. Danish and German
15 study directly address this issue.

16 Why should I ignore? Why
17 should I even bother to worry about other
18 drug contamination issue for this case.

19 Q. Okay. That's helpful. I
20 think you're saying that you didn't look
21 at metformin or Zantac because they have
22 different populations than the valsartan
23 population, correct?

24 A. Yeah. Sir, I don't even

1 know metformin had an issue. I know
2 vaguely about Zantac issue.

3 Q. Okay.

4 A. Even that part I just
5 vaguely know a little bit. I am not for
6 sure how much research I have to be doing
7 to answer your current question about
8 valsartan impurity, right.

9 Q. Right. So when you're
10 thinking about an impurity of NDMA in
11 valsartan, you felt like you didn't need
12 to look at Zantac or Metformin, because
13 they had different populations. They
14 also have a different mechanism as to how
15 NDMA is formed. Did you know that?

16 A. No, I don't.

17 Q. Zantac breaks down -- it's
18 been stated that Zantac breaks down not a
19 manufacturing defect. So it's not in the
20 drug right off the assembly line.

21 Zantac breaks down due to
22 heat, humidity, time, possibly other
23 factors inside of the body.

24 That's what's been stated,

1 right?

2 MR. MERRELL: Objection to
3 form.

4 THE WITNESS: Sir, I'm
5 sorry. Go ahead. I'm sorry, I
6 don't mean to cut you off, I'm
7 sorry.

8 BY MR. NIGH:

9 Q. Do you recall seeing that,
10 that the way in which Zantac gets NDMA,
11 is much different than the way in which
12 valsartan has NDMA, correct?

13 A. No, sir. I'm so glad you
14 learn so much in the past few months,
15 right. And I have no idea what is the
16 underlying process of this contamination
17 works, right, for each medicine.

18 I really admire you for you
19 to learn things so fast, right.

20 Q. But if you were wanting to
21 think about whether or not to consider
22 Zantac epidemiological studies as to
23 whether or not that's beneficial for
24 valsartan epidemiology and the question

1 at hand here, you would want to know that
2 the way in which they're getting NDMA is
3 similar, correct?

4 A. I have no opinion, sir. I
5 am not a toxicologist. Besides, I have
6 not reviewed the papers in detail
7 regarding the Zantac impurity question.

8 I'm not quite sure where --
9 where the question right now, sir. You
10 continue asking me the question about
11 other impurity, right, other drugs, which
12 was not in my assignment, which is not my
13 expertise.

14 I'm not quite sure how I can
15 actually help you on this case to figure
16 out that the valsartan -- we haven't
17 solved the valsartan issue again. Why we
18 actually worried about other
19 contaminants, right.

20 Q. Would you also, in
21 understanding the question between Zantac
22 and the amount of NDMA versus valsartan
23 and the amount of NDMA, that the amount
24 of NDMA that's been reported in Zantac,

1 is much different than the amount of NDMA
2 that's been reported in valsartan.
3 That's something that you would also want
4 to consider as you're thinking about
5 whether or not you look at Zantac epi
6 studies for the question at hand here,
7 right?

8 A. No. I don't think it's
9 relevant. It was not in my assignment.

10 Q. You don't think that it
11 would be relevant -- when you're
12 questioning whether or not to include --
13 you didn't look at Zantac studies, right,
14 Zantac epi studies?

15 A. Sir, my assignment was not
16 regarding the Zantac. My assignment is
17 regarding the impurity in valsartan,
18 right.

19 Q. Right.

20 A. So I don't know that you can
21 transport the findings from Zantac to our
22 current case or not. I have no idea,
23 sir. I cannot say either way, right.
24 I'm not an epidemiologist. I am not a

1 toxicologist. I cannot answer your
2 question.

3 If you can educate me here,
4 I'm happy to learn from you, right.

5 Q. Nonetheless, you looked at
6 Madigan's report, and in thinking about
7 whether or not there's an association
8 between valsartan that's contaminated
9 with NDMA and increased cancer risk, you
10 decided to look at Pottegard and Gomm,
11 not any of the Zantac epi studies,
12 correct?

13 A. The Danish study, German
14 studies are relevant to our current case.

15 Other medicine contamination
16 may be interesting, but it was not in my
17 assignment.

18 Q. What do you mean by it
19 wasn't in your assignment?

20 A. Well, sir, if you read in my
21 Section C, very clearly you helped me
22 this morning even read with me my
23 assignment, right. Does my assignment
24 say anything about I should worry about

1 Zantac impurity? Does it say anything?

2 Q. Let's take a look. Number
3 11. We're going to pull up your expert
4 report. I want to be real clear here.

5 MR. NIGH: Number 11,
6 Page 5. Put that on the screen.
7 Let's blow that up again.

8 BY MR. NIGH:

9 Q. It says, "I have been
10 retained by defendants to provide an
11 expert opinion in the litigation
12 styled" -- and chose valsartan.
13 "Specifically, I was asked by counsel for
14 defendants to review and assess the
15 opinions presented by David Madigan, who
16 submitted an expert report on behalf of
17 the plaintiffs analyzing the results from
18 the dietary and occupational exposure
19 studies to infer potential risk of
20 carcinogenicity from NDME or NDEA
21 impurities in valsartan and to provide my
22 own assessment of those issues."

23 That's what it says,
24 correct?

1 A. Yes, sir.

2 Q. Okay. Now, that assignment
3 says "analyzing the results from the
4 dietary and occupational exposure studies
5 to infer potential risk of
6 carcinogenicity of NDME or NDEA
7 impurities in valsartan." That's the
8 first part of that statement. That
9 statement doesn't include Pottegard or
10 Gomm, correct?

11 A. Correct.

12 Q. The second part says, "And
13 to provide my own assessment of those
14 issues."

15 Is it that part of the
16 assignment that you felt authorized to
17 look at Gomm and Pottegard?

18 A. I said in my report very
19 clearly after I raised some concerns
20 about Dr. Madigan's report, I said, well
21 why don't we actually directly address
22 the issue using the valsartan impurity
23 studies, right, instead of you go to the
24 bypass, somehow take a detour, right,

1 using other studies. So that's what I'm
2 try to. I provide to you two studies
3 directly addressed issue here, right.

4 Q. I understand.

5 A. That's what I'm doing, yeah.

6 Q. You made the determination
7 in your understanding in providing an
8 assessment of those issues, to go to the
9 valsartan epi studies Pottegard and Gomm,
10 right?

11 A. Yes.

12 Q. Why didn't you make the
13 determination to then also look at other
14 medications that were contaminated by
15 NDMA?

16 A. I am not for sure I should
17 do it that way, sir.

18 If I have unlimited time in
19 my life, I wish I can learn a lot of
20 things from you guys. You know, you guys
21 catch things so quickly. I don't catch
22 things very quickly. I need a lot of
23 time to understand the toxicology report,
24 even epidemiology report.

1 Honestly, I have a day job.
2 I cannot afford it, right, to do
3 something is irrelevant to this case.

4 Q. Okay. The last part of your
5 sentence, you said, "Honestly I have a
6 day job, I cannot afford it to do
7 something irrelevant to this case."

8 Did you believe that that
9 would be looking at the other medications
10 that were contaminated by NDMA, those
11 epidemiology studies, looking at those
12 studies, would be something that is
13 irrelevant to this case?

14 MR. MERRELL: Objection to
15 form. Calls for a legal
16 conclusion.

17 THE WITNESS: Well, I
18 apologize, sir.

19 You know, if you think that
20 this is very important, looking at
21 other medicine impurity, I wonder
22 how come your expert witness
23 didn't even take a look at it,
24 right.

1 If they take a look at it,
2 I'd be happy to make a comment
3 about their findings. But they
4 didn't do anything. They didn't
5 even bother to go to valsartan
6 study.

7 I actually made a little bit
8 of effort to bring up to you guys
9 to say, well, two studies directly
10 addressing issue.

11 You said, wow, that's very
12 good. Why don't you go the next
13 mile and figure out what other
14 things like Zantac, Metformin.

15 I said, well, gee, you know,
16 sir, how many contaminated drug in
17 the world, how many drug I should
18 worry about before I submit my
19 report.

20 Sir, this is unrealistic
21 now, right. It is really not
22 relevant anymore.

23 BY MR. NIGH:

24 Q. Now, in your answer, I hope

1 you understand that there -- we have more
2 experts than just Dr. Madigan, right?

3 A. I don't know, sir. I don't
4 know how many experts you have.

5 Q. So you haven't seen the
6 opinions, you haven't seen the reports of
7 Dr. Etminan, Dr. Panigrahy, Dr. Lagana,
8 or Dr. Hecht, correct?

9 A. The only report I read very
10 quickly, not very detailed, was the
11 epidemiologist that you mentioned, right.
12 Other than that, I didn't read the --
13 your expert witness report.

14 Q. Dr. Etminan you reviewed
15 very quickly. Is that what you just
16 said?

17 A. Yes. I did glance over.
18 Because I find out, interesting enough,
19 all his study he recommended Dr. Madigan
20 included. I said well, gee, you know, in
21 that case I don't have to read the
22 epidemiology expert witness, because
23 Dr. Madigan solely depend on the
24 epidemiology. Your other expert read the

1 guidance, right, to say, wow,
2 Dr. Madigan, you should read X, Y, Z.

3 So Dr. Madigan say, oh,
4 yeah, yeah I take it. So in his
5 deposition Dr. Madigan said, Yes, I only
6 consider those documents or papers
7 provided by the epidemiologist. That's
8 my understanding.

9 Q. So as you quickly reviewed
10 Dr. Etminan's report, you believe that he
11 doesn't have Pottegard -- Gomm or
12 Pottegard in his expert report as far as
13 you understand?

14 A. No, sir, I apologize, I
15 don't remember exactly the report
16 anymore. I'd be happy to read it and get
17 back to you.

18 Q. But as you sit here today,
19 you wouldn't be able to say one way or
20 the other, right?

21 A. Correct.

22 Q. And also you wouldn't be
23 able to say one way or the other whether
24 or not Dr. Etminan, plaintiffs'

1 epidemiologist expert, whether or not
2 he's included review of ranitidine
3 epidemiological studies, correct?

4 A. Correct.

5 MR. MERRELL: Counsel, we've
6 been going about an hour and a
7 half. Can we take a break
8 shortly?

9 MR. NIGH: Yeah, can you
10 give me just about two more
11 minutes and I think it will be a
12 good time for a break.

13 MR. MERRELL: Of course.

14 BY MR. NIGH:

15 Q. So I want to see if I
16 understand this correctly.

17 You found it relevant, in
18 terms of the questions here, to look at
19 Gomm and Pottegard, but you did not find
20 it to be relevant or close to the issues
21 at hand, I think you used the word
22 "irrelevant," that is, not a legal
23 conclusion, but you used that word.

24 You found it to be

1 irrelevant to look at ranitidine or
2 Zantac epidemiology or Metformin
3 epidemiology studies, correct?

4 A. I apologize to use the word
5 "irrelevant." That's probably the wrong
6 word to use it.

7 I'm trying to say is my
8 assignment did not include taking a look
9 at other contaminants, right, in other
10 medicines. That's my first answer to
11 you.

12 Second, honestly, I don't
13 have so much time on hand to deal with
14 all other medicines. I have no idea how
15 much other medicine is contaminated, I
16 have no idea. If you ask me, how come
17 you don't do Zantac, Metformin, somebody
18 else would say how come you don't do A,
19 B, C, other drugs. That is the answer,
20 sir.

21 MR. NIGH: Okay. I think we
22 can take a break now. Thank you.

23 THE VIDEOGRAPHER: The time
24 right now is 2:51 p.m. We are off

1 the record.

2 (Short break.)

3 THE VIDEOGRAPHER: The time
4 right now is 3:12 p.m. We're back
5 on the record.

6 BY MR. NIGH:

7 Q. Doctor, I want to ask you
8 about the levels of NDMA that were found
9 in valsartan, okay?

10 A. Yes, sir.

11 Q. Do you know what the levels
12 of NDMA were that were found in
13 valsartan?

14 A. I don't know, sir.

15 Q. Do you have any way of
16 describing the levels of NDMA that were
17 found in valsartan?

18 A. No, sir.

19 Q. Do you have any idea or any
20 way of describing how long the valsartan
21 medications were contaminated for in the
22 U.S.?

23 A. No, sir.

24 Q. So you haven't seen any

1 internal testing or any FDA testing that
2 describes the amount of NDMA that was
3 found in the valsartan drugs, correct?

4 A. The only information I got
5 is like you said for mainly from
6 Dr. Madigan's report.

7 Q. Okay. Well, what do you
8 know in terms of internal testing or FDA
9 testing of the amount of NDMA that's in
10 the valsartan drugs?

11 A. No, sir.

12 Q. You have no knowledge of
13 that, correct?

14 A. No, sir.

15 Q. Okay. And how about the
16 amount of NDMA that was measured in
17 people's diets and the dietary levels?

18 A. I have no idea, sir.

19 Q. So as you sit here, you
20 can't make any statement or comparison of
21 the amount of NDMA that was in people's
22 diets and the dietary studies versus the
23 amount of NDMA found in the valsartan
24 pills, correct?

1 A. Well, I know a little bit
2 about a dietary, the food and recall.
3 You know, for example, someone can ask
4 me, last month, what did you eat, how
5 many strip of bacon you eat, right,
6 something like that. And they
7 extrapolate those kind of things and
8 convert it to the level of exposure.
9 That is only the level I understand, sir.

10 Q. Do you know how many -- how
11 much NDMA that they were reporting in
12 their daily diet in the various quartiles
13 in dietary studies?

14 A. Well, this quartile, some
15 paper they describe the level. So I know
16 the level, but I can't understand
17 biologically how much you are talking
18 about, right, in your body or your
19 bloodstream, whatever you define.

20 Q. Do you know how much NDMA
21 that they were saying was in the foods in
22 those dietary studies, do you have any
23 way of describing that?

24 A. No.

1 Q. So if I were to make the
2 statement that the amount of NDMA found
3 in valsartan pills was as high as 600
4 times the amount of NDMA in a person's
5 daily diet, you would have no way of
6 knowing if that was true or not, correct?

7 MR. MERRELL: Objection to
8 form.

9 THE WITNESS: Yeah, I have
10 no -- I don't know where I can get
11 that information from
12 Dr. Madigan's report.

13 BY MR. NIGH:

14 Q. Is that something you looked
15 for in Dr. Madigan's report and you just
16 didn't find it or you don't recall
17 looking for that?

18 A. Well, he maybe mention
19 something. Maybe if I can read his
20 report again I can confirm. What I think
21 is he did not mention or I forgot what he
22 mentioned. Maybe somewhere he mentions
23 well, valsartan impurity probably is X
24 times higher than whatever is, right.

1 That's probably what he said somewhere.

2 But I need to go back to his report.

3 Q. But as you sit here right
4 now, you don't remember any comparison
5 that Madigan made or that you've seen in
6 terms of comparing the amount of NDMA in
7 the valsartan drugs versus the amount of
8 NDMA in these dietary studies, correct?

9 A. I don't recall, sir.

10 Q. And as you looked at the
11 dietary studies, you don't recall whether
12 or not, when dietary studies had lower
13 amounts of NDMA in the highest quartiles,
14 they were less likely to show effects
15 than when they had higher amounts of NDMA
16 in the quartiles, the highest quartile.
17 Do you recall ever looking at that?

18 A. The analysis Dr. Madigan did
19 most is sort of transport from
20 publication. For example, in a
21 publication, the majority of
22 publications, they compared the quartile,
23 right, the Q1 against the Q2, Q3, and Q4.
24 And most they are reporting on the trend

1 test combining those three tests
2 altogether. That's what Dr. Madigan
3 mainly depend on, right, using those
4 P-values, using this statistical
5 significance job and word, to claim there
6 is issue from this study for this cancer.

7 That's what I'm concerned,
8 from a statistical point of view, is this
9 a valid way to evaluate the safety of an
10 impurity in valsartan.

11 Q. You don't recall looking at
12 dietary studies or even Madigan's report,
13 to see whether or not as dietary levels
14 are lower -- sorry. Strike that.

15 You don't recall looking at
16 dietary studies or even Madigan's report
17 to assess whether or not if the dietary
18 levels are lower in the highest quartile
19 in various dietary studies, then it would
20 be less likely to show an effect than
21 dietary studies that had higher amounts
22 of NDMA in the dietary studies. You
23 never looked at that or saw that in
24 Madigan's report?

1 A. I don't recall, sir.

2 Q. That wasn't something that
3 was important to you in terms of the
4 findings or conclusions that you made in
5 your report, correct?

6 A. I'm sorry. I missed a few
7 words in the beginning. Could you say it
8 again, please.

9 Q. I said that wasn't something
10 that was important to you in the findings
11 or the conclusions that you made in your
12 report, correct?

13 A. Yes, if I didn't say in my
14 report, then it is -- I either say it is
15 not relevant or something I don't think
16 is important.

17 Q. And comparing the amount of
18 NDMA in the valsartan pills compared to
19 the amount of NDMA in the dietary
20 studies, that also wasn't important to
21 you in the findings or the conclusions
22 that you made in your report, correct?

23 A. Well, first I have a concern
24 how can we use the dietary study even

1 infer the issue on the impurity of
2 valsartan. I have a hard time to
3 extrapolate the result from the dietary
4 studies or occupational study to
5 purity -- impurity valsartan study.

6 Q. And you're not a
7 toxicologist, correct?

8 A. No, sir.

9 Q. So you're not commonly
10 experienced in looking at contaminations
11 or carcinogens or toxins in one source
12 and trying to make conclusions or
13 assumptions of that contamination and the
14 amount of that contamination in another
15 source, correct? You don't do that?

16 A. Not for the contamination,
17 but I have involved in many, many Phase I
18 trials for drug development which started
19 with animal study. We figure out is it
20 highly significant, right, for the new
21 compound.

22 But unfortunately when we
23 transported this model to human beings,
24 sadly, most didn't work. We cannot even

1 transport the animal study result to
2 human beings either.

3 That was my understanding
4 beyond the use safety, right, or
5 contaminant. I didn't deal with
6 contaminant issues before.

7 Q. Now, let me rephrase that.
8 I see how you thought of animal studies.
9 So I'm just speaking of human
10 epidemiological studies.

11 You're not commonly --
12 you're not experienced in looking at
13 contamination or carcinogens or toxins in
14 one source of epidemiological studies and
15 trying to make conclusions or assumptions
16 of that contamination and the amount of
17 that contamination in another source.
18 That's not something that you do,
19 correct?

20 A. I don't, but, sir, if you
21 allow me to say one thing. Even within
22 the dietary studies, the studies are so
23 heterogenous, you know, as Dr. Madigan
24 indicated in his report, also deposition,

1 right, even Song, S-O-N-G, paper, the
2 meta-analysis, they actually admitted
3 even the study involving meta-analysis is
4 so different, right.

5 If you look at the forest
6 plot of meta-analysis by Song, you can
7 see it. The effect size, even
8 statistical significance, the changing
9 back and forth around this null value,
10 which is one, odds ratio, or OR.

11 You know, that indicates
12 even with the dietary study, I cannot use
13 the result from the one dietary study to
14 another one, right. Easily it's not
15 applicable.

16 That's why they use
17 meta-analysis, to try to combine the
18 information to go together, get a single
19 summary to tell us if there is something
20 going on with this -- with the
21 contamination.

22 Q. Okay. Let me see if I
23 understand your testimony.

24 I believe you are agreeing

1 with me that you're not experienced in
2 looking at contamination or carcinogens
3 or toxins in one source of
4 epidemiological studies and trying to
5 make conclusions or assumptions of that
6 contamination and the amount of that
7 contamination in another source. That's
8 not something that you do, correct?

9 A. Correct. I don't do that.

10 Q. So I think what you're
11 telling me is your concern is that, even
12 looking at the dietary studies, there's
13 so much heterogeneity and other issues
14 with those studies, that you don't
15 believe you can extrapolate even to other
16 dietary studies, those findings, correct?

17 A. To valsartan, yes. Okay.
18 Yes.

19 Q. Right. Not just to
20 valsartan, but even to other, you know,
21 dietary issues. So if your question was,
22 does NDMA in diet cause cancer? You
23 would raise, there's too much
24 heterogeneity between the dietary

1 studies, and model fit issues and other
2 things of that nature, that you don't
3 think the dietary studies could even
4 answer the question, does NDMA in diet
5 increase the risk of cancer, right?

6 A. Yeah. For a specific
7 population. If you ask yourself, for
8 this particular population, can you tell
9 me I have such contamination for NDMA,
10 right, I say, well, I'm not for sure how
11 to answer your question, right. Even if
12 I use meta-analysis, I cannot, right.

13 Basically we cannot even
14 pre-specify population. You telling me,
15 and those people what is the number, you
16 know, max number, whatever you want to
17 define as the cutoff, ratio or whatever
18 the number is, that is applicable to
19 everyone or to this particular
20 population, right. We don't know. We
21 cannot even use meta-analysis to helping
22 us.

23 Q. When you say population, you
24 don't mean United States, because we're

1 looking at people from the United States,
2 versus other countries, correct?

3 A. Yeah, I'm talking about
4 population. For example Danish
5 population, those are using so-called
6 Danish the -- registry database, health
7 -- so-called health registry. That's
8 their population that they're talking
9 about.

10 Then you talk about the
11 German study. And those guys deal with
12 insurance companies. That's the
13 population that they're talking about.

14 So every study population,
15 they have well defined population, right,
16 of subjects they followed. So that's
17 what I'm talking about in population.

18 Q. So you would have difficulty
19 taking the findings, for example, in
20 Pottegard, a Danish population, and
21 giving meaning to what happens in the
22 U.S. population. Is that what you're
23 saying?

24 A. Yeah. I agree -- agree with

1 that. I'm saying -- you're absolutely
2 right. I cannot saying Danish findings
3 is automatically transportable to U.S.
4 particular population. We don't know
5 that. We have no idea.

6 Either way, I cannot -- like
7 I said before, sir, even with the two
8 studies, we -- we know they directly
9 address the issue, right. However, like
10 every observational study, they had a
11 limitation, right. So we don't know how
12 we can actually say definitely today,
13 sitting here, say impurity of valsartan
14 really caused the problem or not. We are
15 not in a position even to make a decision
16 right now. We really need a very well
17 conducted prospective study, not probably
18 with the valsartan contamination or
19 impurity population because that's
20 impossible to do anymore, right.

21 So that's the issue we're
22 facing. We need to collect more data.
23 And we need more studies.

24 Almost every paper that

1 Dr. Madigan cited in the dietary study,
2 towards the end of the day, you know,
3 there's one line, they said there's
4 limitation. We should conduct a
5 prospective study, a long-term follow-up.

6 That's what they are saying.
7 Unifying words. You know very well,
8 because you read those papers. Worried
9 about words, right.

10 Q. So it's your belief that
11 without that prospective study, it
12 doesn't matter how much contamination
13 there was in the valsartan pills, we
14 wouldn't be able to study the issue,
15 right, because we can't do a prospective
16 study at this point?

17 A. Well, I think what -- if you
18 allow me to say a few words. If I
19 were -- had a choice, having a choice, I
20 said either you follow the Danish
21 population a little longer, right.
22 Unfortunately, those population, the
23 patients will be contaminated by other
24 things, right.

1 Maybe they started eating a
2 lot of food with contamination, et
3 cetera, right. So we do need longer
4 follow-up, even though the study has
5 4.5 years immediate follow-up. It's
6 pretty long.

7 But on the other hand we
8 cannot really go back to do a prospective
9 study anymore with this valsartan
10 impurity, anymore, right.

11 So what I think is the best
12 that we can do at this stage, you
13 actually design a trial, for example
14 using dietary, right. And you say let's
15 use a tactic, just like follow the
16 patient from the beginning for many, many
17 years, right, for dietary. And see how
18 much contamination you are talking about,
19 right.

20 Then you match the dietary
21 population patients closely to your
22 valsartan U.S. population, what kind of
23 patient are taking this impurity
24 contaminate, right, the valsartan. So

1 that would probably give us a signal to
2 find out what's going on.

3 Q. So you would want to design
4 a clinical trial where the patients in
5 the dietary study are being given food
6 that has the amount of NDMA as the amount
7 of NDMA that people in valsartan were
8 getting each day in the contaminated
9 pill, is that what you're saying?

10 A. No, you cannot afford people
11 taking a certain amount of contamination,
12 right. That's not ethical at all.

13 But I'm saying first you
14 need to sort it out, if any association
15 with exposure and unexposure, right, or
16 the level of exposure, using dietary
17 study first, right. You cannot force
18 people, say, hey, you give me the
19 equivalence of food contaminant, right,
20 equivalent to valsartan impurity level.
21 I'm not quite sure you can do that,
22 right.

23 Q. Have you seen anything that
24 suggests that it would take about

1 60 pounds of bacon, eating about
2 60 pounds of bacon a day to get the
3 amount of NDMA in your food that people
4 were getting in one pill of valsartan?

5 A. Well, I don't know. I never
6 heard about that piece.

7 Q. Okay. That's something that
8 you would want to know, right?

9 MR. MERRELL: Objection to
10 form.

11 THE WITNESS: Well, you
12 know, there are so many news this
13 day. I'm just really not sure how
14 true it is.

15 BY MR. NIGH:

16 Q. Well, if you did the math
17 from the FDA, and what they say the
18 amount of bacon and the amount of NDMA is
19 in bacon, and then you looked at the
20 amount of NDMA in valsartan, you could do
21 the math, you could see that it's 30 to
22 60 pounds of bacon. You haven't done
23 that though, right?

24 A. No, I have no idea. Again,

1 I'm not a toxicology or epidemiology.

2 Q. Okay. What do you know
3 about new user designs?

4 A. Well, in the Danish study,
5 the authors did some sensitivity
6 analysis, also called supplementary
7 analysis. And one thing they did are
8 called incident to users. They don't use
9 the word "new users." But anyway, that's
10 a similar term.

11 So they are talking about
12 for the new users they do analysis
13 between the two groups, one is exposed
14 and unexposed. That's my understanding.

15 Q. Right. "New user" and
16 "incident user" are terms that are used
17 commonly to talk about new user design or
18 incident user design, those are used
19 interchangeably, correct?

20 A. Well, we -- it is
21 interesting. I think we use -- incidence
22 is a more mathematical term. And using
23 new user is sort of like ordinary
24 language.

1 Q. Okay. One is more technical
2 you think and the other -- or more
3 mathematical and the other is ordinary
4 language, but they are discussing the
5 same thing, correct?

6 A. That's my understanding,
7 sir.

8 Q. Okay. And is it your
9 understanding that --

10 A. I have some of my -- I'm
11 bleeding.

12 MR. MERRELL: Do you want to
13 take a break?

14 THE WITNESS: No, no, that's
15 okay. I just scratched myself.

16 You talk to lawyers you get
17 nervous, right, so I started
18 scratching. If you allow me to
19 call your first name --

20 MR. NIGH: Sure.

21 THE WITNESS: You are pretty
22 tough lawyer, aren't you, right,
23 you are famous for.

24 BY MR. NIGH:

1 Q. Famous? Oh, like -- Bill
2 Nye the Science Guy.

3 A. Well, anyway. Sorry, I
4 apologize.

5 Q. Okay. Let's take a look
6 at -- my question is, in the last ten
7 years, aren't there, you know, a lot of
8 studies that are out there talking about
9 that it's helpful or useful to do new
10 user or incident user design in
11 observational studies?

12 A. Well, the only thing
13 recently, I did -- helping a company
14 figure out using this so-called EPO
15 equivalent. I don't know if you know
16 this EPO, this compound.

17 We actually helping chemo
18 patients, right, their hemoglobin level
19 is too low, we're giving them this EPO,
20 and it jack up their red cells. Also the
21 hemoglobin level, right. So there is
22 other alternative right now, and I'm
23 helping a biotech company to analyze the
24 data with the so-called incidence

1 dialysis patient. That means there's a
2 newly -- newly go to treatment for
3 dialysis patient.

4 Even in the beginning, they
5 didn't use it, right. Then during the
6 trial start to use it.

7 So we are very interested to
8 find out the incident users they not have
9 any benefit by taking this oral EPO
10 equivalent compound.

11 Q. Okay. Describe the benefits
12 or advantages of using a new user design
13 or incident user design?

14 A. Well, I think somehow, I'm
15 not quite sure in this case, why this
16 incident user becomes interesting.

17 I would say the primary
18 endpoint is for entire population, right.
19 They have 5,000 patients available in the
20 database. That's their primary endpoint.

21 Then afterwards they can do
22 other so-called secondary analysis. For
23 example, this is called a subgroup
24 analysis thing.

1 So they can pick up anything
2 they wanted to, right, the incident users
3 or something else. People do all the
4 time. But see the problem is for the
5 subgroup analysis, we have to be careful
6 how to interpret the results now.
7 Because you cannot use a .05 anymore for
8 all the subanalysis, right. And that
9 will be exactly falling into this
10 multiple comparison problem.

11 So if you talking to people,
12 subsequent analysis, yes or no, people
13 always tell you, you have to make
14 adjustment. To make adjustment, that's
15 exactly the same thing, we talking about
16 the whole day, multiple comparisons,
17 right. So you have to be careful when
18 you interpret a result for all the
19 subgroup analysis.

20 In this case we have to be
21 careful to interpret the incident users,
22 right, what is the hazard ratio, what is
23 it you are talking about, right.

24 And for example, in this

1 case, I believe at a rate of one point
2 something, you know, is not a really
3 pressing hazard ratio.

4 Q. I asked you if you could
5 describe the benefits or advantages of
6 using a new user design or incident user
7 design. Do you know what the benefits of
8 using a new user design or incident user
9 design when looking at observational
10 studies is?

11 A. Well, in general, I have no
12 opinion on this, sir. It is case by
13 case. Depend on what kind of compound
14 you are interested in. If something
15 existing for new users, of course that
16 would be a primary endpoint, primary
17 population, instead of using the entire
18 population you are interested, right.

19 So it all depends on your
20 question you want to answer.

21 Q. Do you believe that the
22 benefits or disadvantages of using a new
23 user design or incident user design are
24 somehow different when it's the primary

1 endpoint or the secondary endpoint?

2 A. Well, I can -- I have a lot
3 of experience dealing with drug
4 development using so-called experience --
5 experience means those patients are
6 already using this compound for many
7 months, or something, right.

8 Now you have a new compound
9 now, right. Then you ask yourself, say
10 do I need to get a naive patient, when I
11 say naive patient means exactly like you
12 said, the new user, right. So when we do
13 a clinical trial, it's always interesting
14 to know, say, are you going to include
15 experienced patient and naive patient.

16 Most of the time we stratify
17 those two populations, right, to
18 understand what happened if the patient
19 had experience with this compound. And
20 it turns out usually experienced patient,
21 their response for the extended treatment
22 is very low. Basically, they already
23 pick it up by those -- the older
24 compound.

1 So in a sense for new users,
2 sometimes you show something -- a big
3 difference between the two groups,
4 treating against control. But
5 experienced sometimes we don't see this
6 very well. The -- I take it back. The
7 other way around. That means the
8 experienced drug, right, the experienced
9 patient using the standard treatment,
10 usually you don't have a very good
11 response, right. But in the new
12 treatment, it's very good.

13 So the difference is very
14 different. But for the new user, usually
15 we don't see too much, because they sort
16 of balance out.

17 So it all depend on what you
18 wanted to do. In this case, it's very
19 interesting. The experienced user, if
20 you think about it, right, they probably
21 getting used to it and this is the
22 thought. So you can ask yourself, if you
23 continue using it, what happened. I
24 think both questions are interesting for

1 this case.

2 But I'm not for sure if you
3 want me ranking which one is more
4 important. I don't know. It depend on
5 investigator or clinical question that
6 you want to ask.

7 Q. In observational studies,
8 what are the benefits or advantages of
9 using a new user design or incident user
10 design?

11 A. For observational study, I
12 don't know, sir. I know as part of the
13 clinical trial setting. I think probably
14 the same principle apply to observational
15 study.

16 I think basically, sir, it
17 all depend on your clinical question,
18 what kind of question you want answered.

19 MR. NIGH: Let's take a look
20 at LP-1578.

21 (Document Marked for
22 identification as Exhibit
23 Wei-11.)

24 MR. NIGH: This will be

1 marked as Exhibit 11.

2 Let's blow up the opinion.

3 BY MR. NIGH:

4 Q. Actually the a the bottom,
5 we can see that this is published in
6 Rheumatology.

7 Do you see that? It's
8 published 2015, Rheumatology.

9 Do you see that?

10 A. Yeah. It's a little too
11 small for me, sir.

12 MR. NIGH: Let's blow that
13 up a little bit more, if we can.
14 We can do each one separately.

15 BY MR. NIGH:

16 Q. Do you see Rheumatology,
17 Nature Reviews Rheumatology, July of
18 2015.

19 Do you see that?

20 A. Yes, sir.

21 MR. NIGH: And now, let's
22 pull up the abstract and the
23 title. Blow up the title. Yeah,
24 right there.

1 BY MR. NIGH:

2 Q. "Opinion: Active comparator
3 design and new user design in
4 observational studies."

5 And you can see the authors
6 there, right?

7 A. Yes.

8 Q. And it says, "Over the past
9 decade, an increasing number of
10 observational studies have examined the
11 effectiveness or safety of treatments for
12 rheumatoid arthritis. Unlike randomized
13 clinical" -- "controlled trials, however,
14 observational studies of drug effects
15 have methodological limitations, such as
16 confounding by indication."

17 Do you see that?

18 A. Yes, sir.

19 Q. "Active comparator designs
20 and new user designs can help mitigate
21 such biases in observational studies and
22 improve the validity of their findings by
23 making them more closely approximate
24 RCTs."

1 Do you see that?

2 A. Yes, sir.

3 Q. Is this the first time that
4 you've seen papers that discuss using new
5 user designs can help mitigate these
6 sorts of biases in observational studies?

7 A. Yeah, this is new to me.

8 Q. Okay. Next, it says -- I'll
9 go to, "This principle helps ensure that
10 treatment groups have similar treatment
11 indications, insinuating both measured
12 and unmeasured differences in patient
13 characteristics.

14 It next says, "The new user
15 study includes a cohort of patients from
16 the time of treatment initiation,
17 enabling assessment of patients'
18 pre-treatment characteristics and capture
19 all events occurring during follow-up."

20 Do you see that?

21 A. Yes, sir.

22 Q. Are you aware that there
23 were numerous studies over the last ten
24 years that talk about using new user or

1 incident user designs in observational
2 studies and the benefits that it
3 provides? Are you aware of that?

4 A. No, sir.

5 MR. NIGH: Let's take a look
6 at another one. LP-1567.

7 (Document Marked for
8 identification as Exhibit
9 Wei-12.)

10 MR. NIGH: This will be
11 marked as Exhibit 12.

12 BY MR. NIGH:

13 Q. Let's take a look at the
14 second page. At the very top, you can
15 see the name of the journal,
16 pharmacoepidemiology and drug safety,
17 published 2013.

18 Do you see that?

19 A. Yes, sir.

20 Q. And it says, in the
21 abstract, "Comparative effectiveness
22 research includes cohort studies and
23 registries of interventions. When
24 investigators design such studies, how

1 important is it to follow patients from
2 the day they initiate a treatment with
3 the study interventions?

4 "Our article considers the
5 question and related issues to start a
6 dialogue on the value of the incident
7 user design in comparative effectiveness
8 research.

9 "By incident user design, we
10 mean a study that sets the cohort's
11 inception date according to patients' new
12 use of an intervention. In contrast,
13 most epidemiological studies enroll
14 patients who are commonly or recently
15 using an intervention when follow-up
16 began."

17 Now with this, Pottegard had
18 the ability to do a new user design
19 analysis. Had they made the decision to
20 make that their primary endpoint, the
21 data would not have changed for that
22 analysis, correct?

23 A. You mean they're going to
24 switch the incident users, the subgroup

1 as the population of interest? That's
2 what you're asking me?

3 Q. Yes. They could have done
4 that?

5 A. Yeah, well, they could.

6 Q. And they would have all the
7 data to have been able to report on what
8 the findings would have been for the new
9 user analysis, correct?

10 A. I believe so. They did a
11 sensitivity analysis using the subgroup
12 analysis.

13 Q. In looking at Page 5,
14 Number 4 -- actually, below, on the left
15 side it shows recommendations for
16 reporting.

17 Do you see that?

18 Recommendations for
19 reporting.

20 And Number 4 shows,
21 "Investigators should conduct sensitivity
22 analyses with varying definitions of
23 incident use to illustrate the stability
24 of findings with respect to validity and

1 precision."

2 Do you see that?

3 A. Yes, sir.

4 Q. And that's what Pottegard
5 did, they had a new user design in their
6 study, correct?

7 A. Yeah. They did a subgroup
8 analysis, a sensitivity analysis.

9 Q. Are you aware of whether or
10 not Gomm had a new user analysis?

11 A. That, I don't know.

12 Q. Okay.

13 MR. NIGH: Okay. Let's take
14 this down. Let's look at
15 Pottegard. LP-1573.

16 (Document Marked for
17 identification as Exhibit
18 Wei-13.)

19 MR. NIGH: This will be
20 marked as Exhibit 13.

21 BY MR. NIGH:

22 Q. Now you spent time in your
23 report talking about the American
24 Statistical Association.

1 Do you remember that?

2 A. Yes, sir.

3 Q. And their criticisms of
4 using P-value of less than .05 as a line
5 in the sand, so to speak, right?

6 A. Yes.

7 Q. In other words, if a P-value
8 in a study is .051 versus .049, those
9 don't have a large difference in how you
10 interpret that study, correct?

11 A. Well, it's more than that.
12 Even you can stretch out a little bit.
13 You know, even say .07 and .04, aren't
14 different enough. Basically, they are
15 the same.

16 Q. Okay. I think you used
17 also, if they are .07 and .04, they're
18 going to have a similar effect.

19 Now -- right? I mean, in
20 terms of your interpretation?

21 A. Hold on. Hold on a second,
22 sir. Sorry to interrupt you.

23 The American Statistical
24 Association, if you read it very

1 carefully, they are just telling us,
2 don't use a single metric, which is P
3 less than .05, to make a black and white
4 claim for the statistical significance.

5 We should utilize other
6 judgment, for example, from clinical
7 input -- clinical input, right, and from
8 subject matter people.

9 And we all know very well
10 when Dr. Madigan in his deposition, the
11 defense lawyer showed us ASA statement
12 line by line. Everything, she ask
13 Dr. Madigan, "Do you agree with ASA
14 statement?" And Dr. Madigan always say
15 yes.

16 Okay. So, basically, he
17 agrees with ASA statement, saying we
18 should not use P less than .05 or
19 95 percent confidence interval, excluding
20 null value or not, to make a decision.
21 And broader, we should look at the entire
22 totality of evidence to make a decision.

23 So that's the point. So the
24 P-value is the what. You know, it's not

1 that interesting. You should provide
2 more information to telling us this case,
3 telling actually a lot of information
4 regarding the impurity of the valsartan
5 or not, right.

6 Q. I understand. In terms of
7 interpreting data from a single study, if
8 it has a P-value of .04 or a P-value of
9 .07, as you spoke, your interpretation or
10 the weight that you give to those,
11 there's no bright line rule that says .05
12 makes the finding important, or under --
13 or over 0.5 makes the finding not
14 important, correct?

15 A. That's correct.

16 Q. Now, if the P-value is .04
17 and the other P-value, versus a P-value
18 of .00001, you don't believe that the
19 American Statistical Association is
20 saying to ignore a P-value of .0001, as
21 you think about the effect that that had
22 in that study, correct?

23 A. Oh no, no, sorry. This is
24 misleading. You see a study with a huge

1 sample size like cardiovascular trial.
2 As you know very well, right,
3 cardiovascular trial, they involve
4 thousands and thousands of patients,
5 right. So even your treatment, the group
6 difference is so small, the P-value is
7 very, very small. Because basically a
8 tiny little difference will grow up the
9 P-value or grow down the P-value, right.

10 Everybody knows the fact, we
11 have the cardiovascular trial, we have a
12 wonderful P-value, but the clinical
13 utility is very little. I can give you
14 many, many examples.

15 But in any event, in a rare
16 disease, for example, the sample size is
17 limited. If I have entire world have 500
18 kids, they have a problem, you said well,
19 I'll tell you what, I use 400 patients in
20 the study.

21 Basically you use entire
22 population now. Even the P-value you
23 know because the sample size, the
24 population size, you're now going to get

1 .0001, but you're going to see clinical
2 utility, right.

3 So I don't think we should
4 have used a P-value of .001, versus .004.
5 .01 is highly significant. It must be a
6 lot of clinical utility, right. It's not
7 true at all. This actually contradicts
8 what we are thinking. That is the
9 problem of using P-value.

10 I bet you a dollar if I ask
11 you to explain to me what a P-value is
12 right now, I think you have a hard time
13 to explain to me, right. Most clinical
14 people have a hard time to understand
15 what a P-value is. Basically, they don't
16 even understand P less than .5, okay. So
17 because the traditional way, in the
18 appropriate way, when everybody using
19 P-value .05 is for convenience.

20 But anyway, sorry for this
21 long response to your question.

22 Q. I wouldn't make assumptions
23 about what I know for P-value, okay? I
24 think that's inappropriate for this

1 questioning.

2 But my question is, as
3 you're considering the weight of a
4 particular study, if a P-value is .04
5 versus a P-value of .0001, you would give
6 more weight to the study that has a
7 P-value of .0001 than you would to the
8 study with the P-value of .04, all things
9 else equal?

10 A. You're saying .04, in the
11 same population, the same treatment, the
12 same control, is that what you're saying?

13 Q. Everything else equal. Just
14 looking at the P-value between those two
15 studies.

16 A. If they are identical
17 studies, one got a .04, and the other one
18 .001, we are in trouble. That means
19 highly significant difference. How come
20 you can translate the first study with
21 .04? Then we have really concern now,
22 right.

23 That means FDA always ask
24 you to do two studies, confirm your

1 so-called significance. Now you are in
2 trouble. One isn't so significant, the
3 other one is mediocre. What are you
4 going to do? It's inconsistent.

5 Q. As you interpret P-values,
6 is it your statement that you don't think
7 that a P-value of .0001 in a study has
8 more effect or more weight than a P-value
9 of .04?

10 MR. MERRELL: Objection to
11 form.

12 THE WITNESS: When you say
13 treatment affect size, you see you
14 go back to clinical utility, or
15 clinical effectiveness, right.

16 Your .001, and you --
17 probably the difference only save
18 the patient a couple weeks, but
19 with huge study, you got a .0001,
20 right.

21 Then you say .04. If I gave
22 you the differences of say, two
23 months, you say wow, which one you
24 really think we have more benefit,

1 is the first study with .04 or the
2 second one with .0001.

3 You see the problem in
4 utilizing P-value as the sole
5 metric to make a decision, you
6 don't have the scientific evidence
7 at all. You basically just tell
8 me the probabilities then, right,
9 which is not very helpful.

10 BY MR. NIGH:

11 Q. So as you interpret the
12 study, and you see a study that has a
13 P-value of .04. And another study -- and
14 I'll be very clear. I'm saying a P-value
15 of .0000001, okay?

16 You wouldn't put more
17 interpretation or more weight on the
18 finding that has a P-value of .0000001
19 than you would the one that has a P-value
20 of .04?

21 A. I need to look at the
22 confidence interval of the two studies.
23 The first one, your confidence interval
24 is very tight. For example, hazard

1 ratio, right. Your hazard ratio is like
2 a .99, right, but because your P-value is
3 so good, your other finding of .998 is
4 still below one. You say, wow, look,
5 this is highly significant. But a hazard
6 ratio of .99, that's almost close to one,
7 right.

8 Then the other one is the
9 confidence interval 95 percent. You say
10 wow, look, the hazard ratio is a .7. The
11 other finding is .95, right.

12 So which one you prefer?

13 You need more -- you need
14 more evidence to enter in the P-value,
15 right.

16 Q. Sure. You would want to see
17 confidence intervals as well. But
18 looking at just the P-value --

19 A. Yeah.

20 Q. -- of .04 versus a P-value
21 of .0000001, you can't make any
22 comparison between the effect you would
23 have just looking at P-values?

24 A. No. You look at a

1 confidence interval, that would tell you
2 exactly the size of the difference. Many
3 times what is the effect of size, what is
4 the effect of size you are talking about.
5 It's not only the P-value matters
6 anymore, right.

7 P-value is giving you the
8 first hurdle. You pass the hurdle. You
9 say, well, you know, it looked like my
10 assumption -- there is no difference
11 between two groups. That's your
12 assumption. You reject this assumption.
13 You say, what is the probability, I
14 observe this extreme value, I observe the
15 hazard ratio of .99, right. What is the
16 chance it is .00001. Because you have
17 thousands and thousands of patients,
18 right, so obviously you can detect a tiny
19 little bit of difference of .99 from one,
20 right. I said who cares, who cares about
21 the difference of .01. But because your
22 sample size is so big, you've got such a
23 good P-value. But I said wait a second,
24 let's look at the size of your -- the

1 group before we jump into the conclusion.

2 Do you think that's more
3 informative than to only use P-value?

4 Q. I think in my question --
5 you keep jumping to changing the effect
6 size. I haven't told you effect sizes
7 yet. I've only asked you to look at
8 P-values.

9 I'm not sure why you keep
10 trying to bring -- hold on, hold on. Let
11 me ask my question.

12 A. Okay.

13 Q. I'm not sure why you keep
14 trying to bring the effect size. It's
15 almost like a gotcha moment.

16 What I'm telling you is, in
17 this next question, since you have
18 difficulty just looking at the P-value
19 and want to run to effect size, my
20 question now is, if the effect size is
21 the same in both studies and one has a
22 P-value of .04, and the other one has a
23 P-value of .0000001, would you interpret
24 those any differently?

1 MR. MERRELL: Object to
2 form.

3 THE WITNESS: Sorry, sir,
4 you are changing your story now.
5 You're saying solely based on
6 P-value multiplication. Now you
7 are telling me the two studies are
8 the same size, right.

9 If the same size, the
10 confidence interval is .04 is
11 wider, right, then the P-value of
12 .001, right. Of course, I said
13 choose the one that is .001,
14 because you already told me they
15 have the same size. That's extra
16 information you're giving to me,
17 right.

18 BY MR. NIGH:

19 Q. Let's take a look at
20 Pottegard.

21 Okay. If you take a look at
22 Page 4. Direct your attention to the
23 bottom of the first page, the writing
24 there. You can see that paragraph there,

1 and on over to the second -- to the left
2 column where it says "Results
3 Comparable."

4 MR. NIGH: If we can blow
5 that up to the next paragraph.
6 Just the next paragraph. I don't
7 need all the rest of that. So we
8 can blow this up bigger.

9 BY MR. NIGH:

10 Q. When you look at this, you
11 can see "Results comparable to the main
12 analyses were found when we stratified by
13 sex and age, whereas a stronger
14 association was seen when we restricted
15 to incident users during the study period
16 (hazard ratio of 1.58 with a confidence
17 interval of .99 to 2.52) 95 percent
18 confidence interval."

19 Do you see that?

20 A. Yes, sir.

21 Q. So they report on a
22 1.58 hazard ratio with a confidence
23 interval that just barely crosses one,
24 correct?

1 A. Yes, sir.

2 Q. And had they set out as the
3 primary endpoint to be new user design or
4 incident user design, they would still
5 have that same finding, hazard ratio 1.58
6 on this population, with a 95 percent
7 confidence interval of .99 to 2.52,
8 correct?

9 A. Yes, sir.

10 MR. NIGH: Okay. We can
11 take this off -- off the screen.

12 Actually, let's put
13 Pottegard back up.

14 BY MR. NIGH:

15 Q. As you looked at Pottegard,
16 did you ever wonder or ask the questions,
17 was there contaminated products that were
18 being announced after the publication of
19 this study?

20 A. I don't know.

21 Q. Okay. The point of
22 Pottegard is to compare uncontaminated
23 group to people who were possibly
24 contaminated or probably contaminated,

1 correct?

2 A. Yes.

3 Q. So already in that study
4 design, we don't have a true test in that
5 study design, because even the people in
6 the test group are defined as possibly or
7 probably contaminated, right?

8 A. Yes.

9 Q. And to the extent that
10 people who are put into the test group
11 that were actually not contaminated, then
12 that would -- that would lead to bias
13 toward the null in the study, correct?

14 A. Let me go little slower.
15 You're saying the control arm supposedly,
16 not a contaminant, that's a control arm,
17 correct?

18 Q. No, no, the test group. The
19 test group is defined -- the test group
20 is defined as possibly or probably
21 contaminated, right?

22 A. Yeah.

23 Q. And so if that test group
24 included patients or subjects who

1 actually did not receive contaminated
2 valsartan, then that would lead to bias
3 towards the null, correct?

4 A. Well, if you already have
5 this idea, the impurity in valsartan is
6 really hurting us, right. You don't know
7 that. You're running around in a circle
8 right now, right?

9 You're saying, well, now
10 suppose this impurity is really hurting
11 us for sure, right. Then you're saying,
12 okay, I tell you what, part of this
13 contaminated group, actually they were
14 not contaminated, right.

15 You already said that you
16 were higher bias against this impurity.
17 You know what I'm saying?

18 If you actually truly
19 believe the impurity in valsartan is
20 harmful, you don't have to do a study.
21 You just say good-bye. I don't need any
22 data.

23 But now you're saying, well,
24 wait a minute, let me just argue with

1 you. If this contaminated group, some
2 people did not have contamination, you're
3 saying that you actually bring this
4 towards null.

5 I say well, you already
6 believe the impurity is hurting people,
7 right. That's your assumption, correct?

8 Q. Do you know what bias
9 towards the null means, as that
10 terminology is used to review
11 epidemiological studies?

12 A. Well, that's statistical
13 terminology. It's not really an
14 epidemiology term.

15 Q. What does bias toward the
16 null mean as you're reviewing
17 epidemiological studies?

18 A. You mean the difference
19 between the two groups tend to be smaller
20 than supposed to be. That's close to the
21 null value. That's what you're saying.
22 It's all common language.

23 Q. Your belief that when using
24 the terminology "bias towards the null"

1 or that certain things would cause bias
2 towards the null, what do you think is
3 meant by that?

4 A. Well, bias towards the null
5 means that you are in favor supporting
6 the null hypothesis. The null hypothesis
7 in your case means impurity in valsartan
8 has no association with cancer incidence.
9 That's your null hypothesis, okay.

10 Now, you are saying, look,
11 if I do an analysis, bias towards null,
12 that means that your analysis result
13 actually helping me to demonstrate there
14 is no association. That's what you're
15 saying. That's what you -- your case you
16 are talking about, right, that's bias to
17 the null.

18 Q. So in an epidemiology study,
19 when certain things occur that would lead
20 towards bias toward the null, what is
21 your interpretation as to bias toward the
22 null in that setting?

23 A. All right. Let me make it
24 clear, sir. I'm not speaking with this

1 so-called degree of contamination or
2 contaminant, whatever you want to use,
3 the word, right. Even the treatment or
4 testing group. You say some patient
5 didn't even take it, the impurity, right.
6 Let's forget about this.

7 In general, in general I say
8 what do you mean by a study biased
9 towards the null? That means that your
10 study result actually helping me to
11 actually saying we cannot reject your
12 null hypothesis, right. It's not very
13 powerful to reject a null hypothesis.
14 That is what exactly you are talking
15 about, bias towards the null.

16 Q. That's not what I'm talking
17 about. So let me explain.

18 When certain things occur in
19 a study and they lead toward bias toward
20 the null in that study, doesn't that --
21 doesn't that infer that you're basically
22 watering down the results towards the
23 null when certain things happen in a
24 study?

1 A. Sir, listen to me. That's
2 exactly I'm saying to you. You lose the
3 power of detect -- you reject the null
4 hypothesis. That's the same thing you're
5 saying.

6 Q. I see. So when you're
7 losing the power to reject the null
8 hypothesis, that would -- that would --

9 A. Yes, that would be -- yeah.

10 Q. When you include subjects in
11 the test group that don't have -- that
12 did not take contaminated valsartan, you
13 would lose power to be able to reject the
14 null hypothesis, correct?

15 A. That's in general term, bias
16 toward the null, sir. That's exactly the
17 same explanation as you did, right. You
18 did it much nicer than I did, right,
19 because people don't understand the
20 power. But you understand.

21 Q. Yeah, let me ask this again.
22 When you include subjects in the test
23 group that do not have or did not take
24 contaminated valsartan, you would lose

1 power to be able to reject the null
2 hypothesis, correct?

3 A. Correct.

4 Q. Now, on the flip side, if
5 you included in the control group,
6 patients who actually took contaminated
7 valsartan, you would also lose power to
8 be able to reject the null hypothesis,
9 correct?

10 A. Yeah. Either way. Either
11 way you have a bias towards null.

12 Q. As you reviewed the
13 Pottegard study, did you understand that
14 even in the way in which they defined the
15 test group, that they would be including
16 patients who never took contaminated
17 valsartan in the test group?

18 A. I don't know that a fact or
19 not. But even suppose hypothetically
20 that happened, but, sir, if you think
21 about any observational study, we have so
22 many confounders. You have so many
23 unmeasured confounders, you probably
24 don't make a good adjustment, make the

1 two groups comparable.

2 You know, this one thing is
3 also a confounder. We have no idea how
4 much confounding effect what you describe
5 to us, right.

6 So this is part of it for
7 observational study, basically have issue
8 now, right.

9 And that's why I said many
10 times, I'm not in the position to say
11 impurity in valsartan has nothing to do
12 with the cancer incidence at this stage,
13 because we don't have a well-conducted
14 prospective study, right. Because that's
15 not the case. So that's what is my
16 position.

17 You can't say, well, the
18 contamination is probably all messed up.
19 I say, well, sorry, that is one of the
20 confounders. Well, you can consider
21 other confounders. I can tell you this
22 is probably not an interesting confounder
23 setting, right, balance between the
24 groups. Probably is nothing, right. So

1 basically I'm not worried about this.

2 Q. Let's -- let's talk about
3 that, the weight of confounding based on
4 the study design.

5 MR. NIGH: Let's pull up
6 "Participants" on the first page.

7 BY MR. NIGH:

8 Q. You don't know -- in terms
9 of understanding the weight of
10 confounding based on the study design,
11 you would want to know how many patients
12 that were contaminated, taking
13 contaminated valsartan, got put into the
14 no exposure group, and then how many
15 people got put into the control group or
16 no exposure, and then how many people who
17 were taking -- who never took
18 contaminated valsartan got put into the
19 test group. Like you don't know -- you
20 don't know the numbers in each of those
21 groups, right?

22 A. Yeah, if you say you switch
23 them around, we don't know how many guys.
24 Actually this is classified. This is

1 very common in clinical study. When we
2 classify those guys, right, yeah.

3 Q. This classification error
4 can be one of the worst errors in a study
5 design, correct?

6 A. No. I disagree. It depend
7 on how much you have a misclassification,
8 right. A tiny little bit doesn't really
9 matter much. Other confounders are
10 probably highly correlated with outcome.

11 Q. I'm glad you mentioned that.
12 It depends on how much misclassification
13 you have, right?

14 A. Yeah.

15 Q. Now, if we look at the
16 study, we can see that the study end date
17 is June 30, 2018, do you see that?

18 "Participants were followed from one year
19 after cohort entry until experiencing a
20 cancer outcome, death, migration, or end
21 of study period (June 30, 2018.)"

22 Do you see that?

23 A. Yeah.

24 Q. If we blow it out, we come

1 back, I'll show the date of this, we can
2 blow that up as well.

3 And we can see the accepted
4 September 9, 2018. Do you see that?

5 A. Yeah.

6 Q. So after June 30, 2018, and
7 after September 9th of 2018, do you have
8 any idea how many products were recalled
9 and found to have contaminated valsartan
10 either with NDMA or NDEA after the
11 conclusion of this study?

12 A. I don't know, sir.

13 Q. Would it bother you if more
14 than 50 percent of the products that were
15 thought to be uncontaminated were
16 actually later found to be contaminated
17 in terms of the study design?

18 A. I don't know the number you
19 are quoting there, sir.

20 Q. Well --

21 A. But I think --

22 Q. -- are you aware that
23 Torrent announced their contamination
24 after the end date of this study, are you

1 aware of that?

2 A. No, sir.

3 Q. Are you aware that Hetero
4 announced their contamination after the
5 end date of this study?

6 A. No, sir.

7 Q. Are you aware that Aurobindo
8 announced their contamination after the
9 end of this study?

10 A. No.

11 Q. Are you aware that there
12 were multiple other companies in Europe
13 that announced the contamination of their
14 products after the end of this study?

15 A. No, sir.

16 Q. Wouldn't that be something
17 that you'd want to know in terms of
18 understanding just how much the
19 misclassification error has impacted the
20 findings of this Pottegard study?

21 A. Well, that's a very good
22 question. How come Dr. Madigan didn't
23 include in his report then. If you think
24 this is such an important issue, how come

1 you don't take to put into the report.

2 Q. Dr. Madigan -- Dr. Madigan
3 is not an epidemiologist. He didn't --

4 A. Well --

5 Q. -- for a reason.

6 A. Okay.

7 Q. Okay? Did you see that
8 Dr. -- - sorry.

9 Did you see Dr. Etminan
10 included this in his report?

11 A. No. I said I just glanced
12 over it. I didn't read it carefully.

13 Q. Did you see --

14 A. But I'm saying --

15 Q. Did you see that several of
16 our other experts also included this in
17 their report or no?

18 A. No, ma'am -- no -- yeah.

19 Q. Okay. You asked why
20 Dr. Madigan didn't include it in his
21 report. But did you see these other
22 experts included that information in
23 their reports?

24 A. Well, sir, my assignment is

1 only dealing with Dr. Madigan's report.
2 I'm not responsible for your other
3 reports, right. Why should I put all my
4 energy -- sorry?

5 Q. Dr. Madigan didn't have Gomm
6 or Pottegard. You made the decision to
7 include Gomm and Pottegard in your
8 report.

9 A. You're telling me, other
10 guys, expert witness, they know the
11 existence of those two studies. How come
12 those guys don't communicate with
13 Dr. Madigan, "Hey, Dr. Madigan, there
14 were two studies that directly address
15 the issue the impurity of valsartan."
16 How come they don't --

17 Q. I don't -- I don't think you
18 understand the purpose of Dr. Madigan's
19 report.

20 Dr. Madigan never gives
21 threshold. He never gives conclusions on
22 causality, correct?

23 A. If there is no causality,
24 what's the point to submit a report?

1 Q. Okay. Did you read his
2 report to get what the point of his
3 report was?

4 MR. MERRELL: Object to
5 form.

6 THE WITNESS: Yeah, I mean,
7 he basically told us that there's
8 an association from the dietary
9 study, from an occupational study.
10 But he admitted he couldn't even
11 translate association to
12 causality.

13 But here you are. You're
14 looking for causality. You say,
15 sorry, I cannot answer your
16 question because basically I
17 cannot answer causality question.

18 I say, wow, okay, why do we
19 need to bother Dr. Madigan, he's a
20 busy guy, to write a report,
21 right.

22 If your epidemiologist can
23 answer this question, why do you
24 need Dr. Madigan then?

1 BY MR. NIGH:

2 Q. Why do you think we used
3 Dr. Madigan?

4 A. I don't know. I'm very
5 curious. I mean, if he in his deposition
6 said, ma'am, we cannot answer causality
7 question.

8 The first thing I said,
9 well, good-bye. If you cannot answer
10 causality, why should I need you on the
11 panel, right?

12 Q. So you would discard his
13 conclusion because he's not answering the
14 question of causality? You would say
15 good-bye, why should I need you on the
16 panel?

17 A. Sir, don't put your word in
18 my mouth. I'm trying to say he couldn't
19 even establish association. And then he
20 had admitted in public he cannot answer
21 the causality question, okay.

22 So my question for you, if
23 you cannot even say the impurity of the
24 valsartan caused the cancer, then what is

1 the point for whole case then?

2 Q. Do you believe that you can
3 answer the causality question?

4 A. Sorry?

5 Q. Do you believe that you can
6 answer the causality question?

7 A. I can't. That's why I don't
8 work for you, unfortunately. You know,
9 you're a very good lawyer. I know there
10 is a problem. We cannot establish
11 causality.

12 If I can, sir, you know, I'd
13 be famous. I would get a Nobel Prize
14 winner. Nobody actually can jump in
15 association to causality that easily.
16 You need clinical input. You need all
17 kinds of people, toxicologists, right.
18 You cannot rely on statistician to tell
19 you there's a causality.

20 Q. Okay. So are you admitting
21 in public now as well that you cannot
22 provide a causality opinion either?

23 A. I didn't say any causality,
24 sir. I didn't say any causality. I

1 didn't helping you to say, well, impurity
2 cause cancer.

3 Q. You don't have a causality
4 opinion one way or the other though,
5 right?

6 A. Why should I need another
7 part? I cannot even establish an
8 association between the impurity and the
9 cancer risk. I cannot even demonstrate
10 either way. How in the world we can
11 actually jump into the wagon and say
12 there's a causality.

13 For my part in this, there's
14 no causality issue at all.

15 Q. Did you review
16 Dr. Panigrahy's report at all?

17 A. No, I don't think so.

18 Q. Okay. So as far as you
19 know, sitting here today, you have no
20 criticisms of Dr. Panigrahy's report or
21 the LCEs that he calculated, correct?

22 A. You mean Dr. Madigan
23 computed LCE?

24 Q. No. No. My question was

1 not about Dr. Madigan. It's about
2 Dr. Panigrahy.

3 As far as you know, sitting
4 here today, you have no criticisms of
5 Dr. Panigrahy's report or the LCEs that
6 he calculated, correct?

7 A. I didn't read his report.
8 How in the world I can say I criticize or
9 not criticize. It's not a logical
10 question, right?

11 Q. I think it's a logical
12 question. I think you're agreeing with
13 me.

14 Because you never read his
15 report, you don't have any criticisms
16 regarding Dr. Panigrahy's reports or the
17 LCEs that he calculated, correct?

18 A. Better way to say, I have no
19 opinion of this. I don't say I'm not
20 going to criticize. Which way -- because
21 I don't know which way he did. So I have
22 no opinion. I cannot make any comments.

23 If that's a better way to
24 answer your question?

1 Q. Yes.

2 MR. NIGH: Okay. We've been
3 going on for a little bit more
4 than an hour. Let's go ahead and
5 take a break at this time.

6 THE VIDEOGRAPHER: The time
7 right now is 4:24 p.m. We're off
8 the record.

9 (Short break.)

10 THE VIDEOGRAPHER: The time
11 right now is 4:44 p.m. We're back
12 on the record.

13 BY MR. NIGH:

14 Q. Now, Doctor, in your report,
15 you provide no information on the
16 background rate of exogenous NDMA from
17 sources such as diet, beer, or smoke,
18 correct?

19 A. Correct.

20 Q. And in fact, that's
21 something that you hold no opinion about
22 or you don't have any knowledge in terms
23 of the amount of nanograms or the amount
24 of exposure that people have to exogenous

1 NDMA from diet, beer, and smoke, correct?

2 A. Yeah. I have a hard time
3 even past the first hurdle, association
4 question. I think the next step, I can't
5 even understand how we can establish.

6 Q. And also in terms of
7 endogenous NDMA, you have no
8 understanding or any -- you haven't
9 looked at any materials that describe or
10 explain the amount of endogenous NDMA or
11 even endogenous nitrosamines, correct?

12 A. Correct.

13 Q. Okay. Let's take a look at
14 your report.

15 MR. NIGH: It's LP-1557
16 we're going to take a look at Page
17 17. Actually Page 10, Paragraph
18 21.

19 BY MR. NIGH:

20 Q. Here you say, "Even if we
21 can claim we collected all of the
22 relevance patients' baseline factors, the
23 modeling of the adjustments for those
24 factors may be questionable since the

1 standard lack of fit test for the model
2 fitting does not provide clinically
3 meaningful interpretation via a P-value
4 of the test."

5 Do you see that?

6 A. Yes, sir.

7 Q. Do you recall giving similar
8 opinions both in Taxotere and Celebrex as
9 this?

10 A. Sir, I don't recall.

11 Q. Okay. Next you say, "For
12 example, in a publication by Dr. Madigan,
13 heavily cited in his report, Loh, et al.,
14 claimed that dietary NDMA intake was
15 significantly associated with increased
16 cancer risk in men and women via Cox
17 proportional regression, adjusted for
18 age, sex, BMI, cigarette smoking status,
19 alcohol intake, energy intake, physical
20 activity status, education level, and
21 menopausal status in women."

22 The Loh study adjusted for
23 numerous potential confounding factors,
24 correct?

1 A. They tried. Dr. Loh was
2 trying. Was trying.

3 Q. Now, what you say next is,
4 "However, it is not clear a thorough
5 model fitting assessment was conducted."

6 Do you see that?

7 A. Correct.

8 Q. You next say, "If the Cox
9 model does not fit the data well, it is
10 known that the resulting hazard ratio
11 does not have clinically meaningful
12 interpretation."

13 And you put, "For this
14 situation, the conclusions of the study
15 and inferences drawn by Dr. Madigan based
16 on the study would be invalid and
17 inherently unreliable."

18 Do you see that?

19 A. Yes, sir.

20 Q. Are you stating that Madigan
21 shouldn't rely on Loh because it is not
22 clear a thorough model fit assessment was
23 conducted?

24 A. Well, sir, this is beyond

1 Loh's paper. Almost every paper, study,
2 Dr. Madigan cited in his report. Sort of
3 lack of assessment of a model fitting.

4 Q. I understand. I'm asking
5 you just in regards to Loh. Are you
6 stating that Madigan shouldn't rely on
7 Loh because it is not clear a thorough
8 model fit assessment was conducted?

9 A. That is my opinion.

10 Q. You recognize that the vast
11 majority of observational studies do not
12 include in the study or provide a
13 comprehensive description of model fit
14 assessment, correct?

15 A. I'm sorry, sir, you say most
16 observational study won't including --

17 Q. I'm saying you recognize
18 that the vast majority of observational
19 studies do not include in the study or
20 provide a comprehensive description of
21 model fit assessment, correct?

22 A. Well, at least for those
23 papers that I read, they didn't give us a
24 very thorough assessment. I don't know

1 in general, sir.

2 Q. Well, in general,
3 approximately what percent of
4 observational studies do you believe
5 provide a comprehensive description of
6 model fit assessment?

7 A. I don't know. But for all
8 the studies Dr. Madigan cited, I look at
9 carefully. I couldn't find it. I mean
10 that only concerned me. I don't really
11 concern about other observational
12 studies.

13 Q. You don't know whether or
14 not the vast majority of observational
15 studies provided do not provide a
16 comprehensive description of model fit
17 assessment?

18 A. Well, sir, if they didn't
19 provide it, that means that the result is
20 not believable, right.

21 Q. So --

22 A. That's a common --

23 Q. Go ahead, you can finish.

24 A. It is common sense, sir. If

1 you cannot tell me if the model
2 adequately fit your data. I said, well,
3 can you tell me -- in fact, you need a
4 validation set, right, to help me, the
5 model is okay or not. You cannot use
6 only one single independent data. The
7 independent data set you fit in the
8 model, right, Cox model in this case, but
9 you have to use another independent
10 observational study to validate the model
11 before clear or not. That is a well
12 known fact now, right. The training, the
13 validation set independent of datasets.

14 Q. Let me be a little more
15 clear about my question.

16 When I am talking about vast
17 majority of observational studies, I
18 don't just mean these dietary studies. I
19 mean the vast majority of observational
20 studies that are done do not include in
21 the study or provide a comprehensive
22 description of a model fit assessment,
23 correct?

24 A. Well, sir, I don't know

1 exactly the percentage you make in this.
2 But I'm really sorry to see that, right.
3 You are very smart lawyer.

4 If you're actually doing a
5 study without validating your assessment
6 appropriate of model, how can you sell
7 your model to outside world?

8 Right. I mean there are
9 tons of papers, they all junk papers,
10 everybody knows that. Right. You
11 publish a paper with all kinds of
12 confounding, you can find out go fishing
13 trip, or whatever, cherry-picking, you
14 pick out a set of variants, you make
15 adjustment, you got a decent P-value and
16 say I'm done. You see that's the
17 problem, right.

18 If you cannot tell me your
19 model is okay, you can do anything you
20 want to, tell me the story. I don't even
21 know if the story is okay or not okay,
22 right.

23 Q. So if the vast majority of
24 observational studies do not provide a

1 comprehensive description of model fit
2 assessment, then you would disregard
3 those studies?

4 A. Yeah, basically I think we
5 don't really believe this kind of study
6 anymore, right.

7 I mean, you know, you are a
8 good law firm. Dr. Madigan is a
9 distinguished statistician. And we need
10 a very high standard, right, to conduct
11 an analysis of observational study,
12 right.

13 Model checking is very
14 important step. Without it, we cannot do
15 anything, right, down the road.

16 Q. And in the absence of that
17 very high standard of conducting an
18 analysis of observational studies, you
19 believe that you cannot demonstrate an
20 association between NDMA and -- NDMA in
21 the diet and cancer, correct?

22 A. Yeah, I can play game with
23 you, say, doctor. You see the Loh paper,
24 he lists so many so-called covariates,

1 right, which is baseline variables.

2 If I have raw data, I can
3 play game and delete some covariates in
4 the model or adding something else, he
5 didn't include it. I bet you I probably
6 can play the game with you, turns out my
7 P-value is greater than .05. But that's
8 an association problem, right. That's
9 the problem.

10 Everybody can manipulate a
11 model and tell you a story. They want
12 you to listen to story.

13 Q. Is that your belief, that
14 Loh could have played games and simply
15 gotten a P-value that was greater than
16 .05?

17 A. Sir, this is so common.
18 That's why it will be hazard ratio is so
19 low. Usually we say, well, look, you can
20 manipulate your adjustments, okay, you
21 can make adjustment and make your P-value
22 significant. We can make adjustment,
23 make your P-value not as significant,
24 right. That's a well known fact. That's

1 why people usually don't believe
2 observational study.

3 It's like for example,
4 Covid-19, the pandemic, right, in the
5 beginning people submit all kind of
6 observational studies, say oh, yeah, you
7 know, this treatment is great, especially
8 our former president, right. He said
9 without any evidence, hey, let's see,
10 this observational study show you this is
11 very good treatment. It turns out in the
12 clinical trial, we don't see anything.

13 So you see, the society now,
14 they don't believe observational study
15 for the Covid-19 anymore. You say
16 without a clinical trial, forget it, I'm
17 not going to use your treatment, even if
18 you have observational studies that will
19 state the statement of fact.

20 See, this is what happened,
21 right, in the last 18 months. You know
22 better than I do, right.

23 Q. All right. Let me see if
24 I've got your testimony right.

1 In general you believe that
2 you can't believe observational studies,
3 correct?

4 A. If you have really nice
5 recent protocol, pre-specified
6 adjustment, then I have a training set to
7 fit in your model. I have a validation
8 set to validate what you claim the model
9 is okay or not. Then I believe you have
10 a story to tell. You have a valid story
11 to tell us, right.

12 But right now, like you say,
13 I don't even give you the details, how do
14 I select this baseline covariates with
15 adjustment. How do I select the spec? I
16 have no idea how you select. How many
17 covariates are you not including in the
18 covariate adjustment. I don't know,
19 right. You just publish.

20 Now, papers that are
21 published in the -- very few people even
22 pay much attention. Very small group of
23 people, oh, yeah, yeah, yeah, this is
24 interesting. But in reality, people

1 don't take this seriously without a
2 rigorous assessment of your model of what
3 your process you are talking about,
4 right.

5 The -- this is actually --
6 you know, we need to hold a high
7 standard, right, for this legal case.
8 You can't set a legal case example in the
9 future. How do we defend the people,
10 right. You have to defend the people in
11 the right way, correct way.

12 Q. Are you aware that most FDA
13 recalls have been prompted as a result of
14 observational studies and not clinical
15 trials?

16 A. I don't recall, sir.

17 Q. Have you ever seen data that
18 demonstrates that?

19 A. I saw many cases FDA had
20 some concern about safety issue of -- for
21 example, and you finish Phase III trial,
22 right, you want to demonstrate your
23 treatment is okay. But FDA still
24 concerned about the long-term toxicity

1 profile. Usually they ask the company to
2 do a marketing Phase IV trial to figure
3 out, do you have the safety issue.
4 That's very common. You know, for
5 example, we did that important E-P-O,
6 EPO, 2000 -- 11 years, to actually sadly
7 say EPO is not safe.

8 Q. Right.

9 A. So you see people doing
10 that. But I don't know exactly for this
11 case, sir, any like contaminant or
12 impurity in valsartan and what the FDA
13 did, I don't know.

14 Q. In general, have you ever
15 seen data that most FDA recalls have been
16 prompted as a result of observational
17 studies and not clinical trials?

18 A. Well, that's why people
19 criticize the result, right.

20 Q. I'm sorry. That's why
21 people criticize the FDA recalls?

22 A. No, no, no. You're saying
23 the observational study was conducted
24 because the recall. And most of the

1 people actually say, well, it's okay.
2 You're telling me, I don't really believe
3 you, right, whatever you say. You know,
4 they don't take it seriously right away.

5 So that's what happened in
6 this society. You can publish any paper
7 you wanted to. In fact, my friend, is a
8 JAMA Open associate editor for
9 statistics.

10 He said -- he told me a few
11 months ago, he said that he got lots of
12 papers for different legal case for
13 safety stuff. Everything is
14 observational study, right.

15 He was so surprised. People
16 manipulate the modeling and actually
17 picking up the model they like and write
18 a paper.

19 So the editors very
20 carefully now to select those papers.
21 They just want to use JAMA, for example,
22 as a vehicle to tell all sides my drug is
23 safe or not safe.

24 He decide -- it's not only

1 for safety issue. If someone wants to
2 badmouth the other drug company, they
3 also publish papers. So this whole world
4 is flooded with not reliable and
5 misleading studies.

6 But people publish. If you
7 pay for it, this case, you can publish
8 your papers.

9 Q. In general, have you ever
10 seen data that most FDA recalls have been
11 prompted by observational studies and not
12 clinical trials?

13 MR. MERRELL: Objection to
14 form. Asked and answered.

15 THE WITNESS: I don't
16 recall. I don't know, sir. In
17 this moment, I don't know.

18 BY MR. NIGH:

19 Q. I believe it's your
20 testimony that even if the vast majority
21 of observational studies do not provide a
22 comprehensive description of model
23 fitness assessment, you would not give
24 reliability to those observational

1 studies, correct?

2 A. I would put very little
3 weight on their findings.

4 I don't really trust the
5 result with just single study. I
6 probably need a validation study.

7 Q. Well, I mean, even if there
8 are numerous observational studies, but
9 numerous observational studies on an
10 issue and none of them provide a
11 comprehensive description of model
12 fitness assessment, you would throw out
13 or ignore the results of all those
14 studies, correct?

15 A. I say I don't even care if
16 they published those papers or not. I
17 don't take it seriously.

18 Q. So you would ignore those
19 results, correct?

20 A. Yeah, unless they have
21 another independent study validating what
22 they are claiming, right. Then I say,
23 okay, that's correct.

24 Q. So in this situation, when

1 Loh doesn't tell you in the study whether
2 or not it used a thorough model fitting
3 assessment, you would ignore the results
4 of Loh, correct?

5 A. I would probably say I'm not
6 going to take this seriously.

7 Q. Okay. Okay. Now, let's
8 take a look at Zheng. You have the same
9 -- your next paragraph, you say, "As
10 another example about the adequacy of
11 modeling, in the paper by Zheng, multiple
12 logistic regression models were
13 utilized." And then you put again, "It
14 is not clear if the model fits the data
15 well. Again, a lack of fit test for
16 model fitting is not informative since it
17 only provides a P-value."

18 And so again, because Zheng
19 does not provide a thorough model fitting
20 assessment in the study as to whether or
21 not that was conducted, you would ignore
22 the results of the Zheng study, correct?

23 A. I wasn't excited about the
24 results at all.

1 Q. You would give it little to
2 no weight, correct?

3 A. Yeah.

4 Q. And in fact, many of the
5 dietary studies here that did not make it
6 clear that a thorough model fitting
7 assessment was conducted, you would have
8 ignored those dietary studies or given
9 them little to no weight, correct?

10 A. Correct. But, sir, you
11 notice some dietary studies are very,
12 very old, right, more than 20 years. And
13 at that time probably those guys were not
14 educated well or trained very well
15 statistically speaking. They probably
16 didn't do it. Okay.

17 But I believe a good well
18 conducted observational study this date,
19 they probably do a very good thorough job
20 to assess the adequacy of the model
21 fitting.

22 Q. I'm sorry. Many of these
23 dietary studies are not published more
24 than 20 years ago. There's many of them

1 that are more recent, right?

2 A. You have one paper published
3 in 1999, right?

4 Q. I know, but many of these
5 dietary studies, we've got some that are
6 published in 2019, 2012, 2011, 2012 --
7 20 -- 20 -- you know, many of these are
8 published in the last decade, correct?

9 A. Yeah.

10 Q. But even then, if they
11 didn't specifically put in the study and
12 describe, make it clear that a thorough
13 model fitting assessment was conducted,
14 then you would have ignored it or given
15 it little to no weight, correct?

16 A. Yeah, I wouldn't pay much
17 attention to it.

18 Q. Isn't that the main problem
19 in terms of your concern about whether or
20 not there's association between dietary
21 studies and the NDMA in diets and whether
22 or not they have an increased risk of
23 cancer? Isn't that your main concern,
24 that they didn't include model fit, and

1 as a result you've given little to no
2 weight or ignore them?

3 A. Sorry. Go ahead, sorry. I
4 don't mean to --

5 Q. That was the end of my
6 question.

7 A. Okay. No, sir. This is a
8 part of it, right. You can see my
9 report. I have several concerns, right,
10 more than just the model fitting stuff.
11 My concern also, saying the
12 decisionmaking about so-called
13 statistical significance and we should do
14 better job than that, right.

15 Even if you have correct
16 model, you should providing more than
17 P-value for that application. That's
18 another concern I have.

19 The third one is more
20 serious. I said even if I believe what
21 you're saying from these publications,
22 how can we actually convince people you
23 can extrapolate the result from the
24 dietary study or occupational study to

1 the impurity in -- in valsartan, right,
2 the issue we are dealing with right now.

3 That's the issue and my
4 concern.

5 Q. Yeah, but you don't -- you
6 don't -- you don't do that sort of work,
7 where you extrapolate results from one
8 exposure to another exposure setting,
9 correct?

10 A. I think we have to be very
11 careful to actually figure out how we can
12 use one type of study, and we can
13 extrapolate the result to another
14 compound. It's not relative to
15 valsartan, right.

16 And you cannot just directly
17 say, well, we see from association from
18 dietary. It is not automatically
19 claiming we have issue with valsartan.

20 Q. Yeah. My question is not
21 that. My question is really about your
22 experience and the work that you do.

23 You don't do that sort of
24 work where you extrapolate results from

1 one exposure setting to another exposure
2 setting, correct?

3 A. Oh, we do. We do sometimes
4 from clinical trial result. For example,
5 in a cardiovascular trial, the patient
6 usually is male patients, right. And
7 especially in old age, very few female --
8 very few female patients involved.

9 So we actually very
10 seriously need to know what the treatment
11 effect the female patient would uptake,
12 right.

13 So we actually utilize the
14 entire study helping us to understand
15 that extrapolation. But we try to do a
16 good job, saying we establish a model for
17 prediction for women, right with the
18 baseline covariates.

19 And then we validate it.
20 And then we apply this model with one
21 dataset to another one.

22 So we do -- we do actually
23 do this kind of work. But you have to be
24 careful to convince people you can

1 transport your model from one study to
2 another one, right.

3 Q. So the model that you're
4 talking about in the work that you've
5 done would be looking at exposure in male
6 patients and how that could be
7 extrapolated to exposure in female
8 patients, correct?

9 A. Yeah. That's a part of one
10 study we did before.

11 Q. You're not talking about
12 exposure in one setting and extrapolating
13 to exposure in another setting, correct?

14 A. No, not that I recall.

15 Q. Okay. For Loh and Zheng,
16 other than model fit, did you have any
17 other criticisms of those studies?

18 A. Sir, this is just the two
19 examples, you know, we can go over all
20 the papers, publications that Dr. Madigan
21 cited.

22 Most of the paper, just to
23 follow the same -- like you're saying,
24 the majority of paper, they didn't even

1 bother to evaluate how good the model is,
2 right.

3 So those older publications,
4 they sort of lack this kind of assessment
5 and process. So it's not only for those
6 two papers, by the way.

7 Q. Other than Loh -- you know,
8 for Loh and Zheng, did you have any other
9 specific criticisms of those studies?

10 A. Oh, other studies -- oh,
11 these two particular studies that you're
12 talking about?

13 Q. These two studies, any other
14 criticisms of those two studies?

15 A. Well, I don't know they
16 actually use -- you see, Counsel, I
17 wanted to share with you, if you go back
18 to the Loh covariate adjustment, right,
19 you can come up how many covariates they
20 make adjustment. If you have 11 or
21 12 covariates adjustment, for example,
22 for sake of argument, you put age as
23 adjustment, right, and the question is do
24 you think age squared is also an

1 important adjustment. You say we don't
2 know.

3 How about age cubed, do you
4 need to make adjustment. Do you think
5 actions among the 11 covariates will be
6 included in the model?

7 You see, model is a
8 simplified version of the truth. The
9 true model is so complex. We actually
10 try to approach the true model with a
11 simplified model.

12 Now the question is can we
13 actually assess your simplified model,
14 actually close to the truth, right.

15 So you see, you can see the
16 Loh and also Zheng papers, right. You
17 say, well, I don't know, like we call
18 kitchen sink, right. And do whatever the
19 result are coming up, right. That's what
20 people usually do.

21 You see, they say well,
22 let's put everything in this disposal and
23 see what happens. It's not a way to do
24 business or scientific investigation.

1 If you want to use those
2 papers as legal cases, you know, please
3 do, but how in the world we can believe
4 one informing a thing, I don't know how
5 many people would believe it. That's my
6 point.

7 Q. So your point is you believe
8 that Loh and Zheng may have over adjusted
9 the findings, included too many
10 covariates or confounders that they
11 adjusted for? Is that what you're
12 saying?

13 A. No. Could be under. Who
14 knows? Basically, I don't know what is
15 the right adjustment. You need a
16 validation set to tell me, yes, this is
17 right amount of adjustment. You cannot
18 adjust to put everything in the sink,
19 say, listen, let's do it.

20 You know, people in the real
21 world, they have hundreds and hundreds of
22 covariates, right. They say using this
23 machine, learning the process. Well,
24 let's see what's going on. They end up

1 with a model. They say, well, okay,
2 believe it or not, this is my model.

3 I said, hold a second, if
4 you cannot validate this model, nobody is
5 going to believe you.

6 So that's the trend this
7 day, sir. You know, unfortunately the
8 dietary papers are such older papers
9 probably mostly right. They didn't even
10 bother -- in the modern world if you
11 don't have validation of the model,
12 nobody will even believe you. If you
13 read a medical journal, everything
14 they're talking about modeling, they have
15 the validation set, independent
16 validation set, right.

17 So though you can see the
18 trend, the people really want to have a
19 valid scientific sort of conclusion from
20 your study.

21 Q. There are many modern
22 observational studies that are published
23 that do not include a clear thorough
24 model fitting assessment described in the

1 studies, correct?

2 A. Well, if you find a paper in
3 New England Journal of Medicine or JAMA,
4 I would be very surprised, okay. But if
5 you find it published in a mediocre
6 journal, anybody can publish this space,
7 as long as you pay a few thousand
8 dollars, right, you can publish. A
9 publication doesn't mean this is a valid
10 argument, right. It's not credible.

11 Q. Okay. So let's take New
12 England Journal of Medicine or JAMA.

13 You recognize that there are
14 many modern observational studies that
15 have been published in the New England
16 Journal of Medicine or JAMA that do not
17 include a clear thorough model fitting
18 assessment described in the study,
19 correct?

20 A. Well, give me example. In
21 the past six months, what kind of paper
22 are you talking about?

23 Q. How many examples do you
24 want?

1 A. Yeah? Well, the example --

2 Q. How many examples do you
3 want to recognize that there are many
4 modern observational studies that have
5 been published in the New England Journal
6 of Medicine or JAMA that do not include a
7 clear thorough model fitting assessment
8 described in the study, how many
9 studies --

10 MR. MERRELL: Object to
11 form.

12 BY MR. NIGH:

13 Q. -- do you want to prove that
14 point?

15 A. Well, it doesn't matter. If
16 you give me a couple of really high
17 profile observational studies without
18 validation, I will be very happy to write
19 a letter to associate editor. I know
20 those guys very well. I say how in the
21 world you guys publish this junk paper,
22 okay.

23 You tell me. You pick a
24 couple of papers. I'm going to tell my

1 friend, say you guys better do a better
2 job.

3 Q. Okay. Taking a look at
4 Page 12, Number 23 in your opinion. You
5 say, "Moreover, for the papers in
6 meta-analysis cited by Dr. Madigan, it is
7 not clear if the authors for the
8 individual papers in the meta-analysis
9 had carefully checked the adequacy of the
10 models utilized in the analysis. Without
11 such analysis, the conclusion of the
12 meta-analysis and inferences drawn by
13 Dr. Madigan based on the meta-analysis
14 would be invalid and inherently
15 unreliable."

16 That is rarely done for any
17 meta-analysis of observational studies,
18 correct?

19 A. That's why we got so many
20 meta-analysis papers floating around in
21 this world, counsel. You know, how many
22 do you believe is a result of
23 meta-analysis? I think of very few.

24 Q. Can you name one

1 meta-analysis of observational studies
2 that has carefully checked the adequacy
3 of the models of all the studies that
4 were utilized in its analysis?

5 A. Well, you can check New
6 England Journal of Medicine. We can go
7 through tomorrow. We can get online to
8 check all the recent New England Journal
9 of Medicine -- meta-analysis New England
10 Journal of Medicine published.

11 I'll tell you the truth, New
12 England Journal of Medicine doesn't
13 publish any meta-analysis papers anymore
14 in the past two years anymore, because
15 they don't believe in meta-analysis,
16 right.

17 Then you say well, this is
18 not fair. You say other journals publish
19 meta-analysis. I say well, gee, you
20 know, look at the high standard of the
21 journal. They actually don't believe
22 this meta-analysis anymore.

23 After they published the
24 Vioxx meta-analysis everything -- no, I'm

1 sorry, it's for the GSK, Tanzeum, right,
2 so-called antidiabetes drug, and they
3 publish meta-analysis about maybe
4 12 years ago, maybe more than that. That
5 was last paper.

6 New England Journal of
7 Medicine published meta-analysis, they
8 learned a bad experience from publish
9 that paper.

10 You can tell me if The New
11 England Journal of Medicine has published
12 a meta-analysis in the past few years,
13 I'll be very happy to share with my
14 associate editor friend at New England
15 Journal of Medicine. I say, gee, how
16 come you guys change your policy.

17 Q. Can you name one
18 meta-analysis of observational studies
19 that has carefully checked the adequacy
20 of the models of all the studies that
21 were utilized in its analysis?

22 A. I don't know exactly there
23 is one. You are a high standard lawyer.
24 You don't want to go with those people,

1 what the majority say, hey, those guys
2 are not very good. So if the majority of
3 people are not very good, it's okay.
4 But, sir, that's not okay, right.

5 You like to be in the small
6 minority, you do a good job. You have a
7 high standard. You actually set a good
8 example for next generation, correct?

9 Instead of using -- say,
10 hey, listen, nobody is doing this, so I
11 don't have to do it. Why do we do that.
12 If society goes what you are trying to
13 do, we are in trouble. We cannot find
14 truth anymore, right.

15 Why do you want to say
16 majority guy didn't do it, so I didn't do
17 it. But you know they are not correct.
18 Why even bother to say I want to mingle
19 with those guys.

20 Q. So is it your testimony that
21 you cannot name one meta-analysis of
22 observational studies that has carefully
23 checked the adequacy of the models of all
24 of the studies that were utilized in its

1 analysis?

2 A. Yeah, most meta-analysis I
3 dealing with using clinical trial result,
4 individual study. So in that case you
5 don't have to make adjustment, because
6 basically they are balanced, right,
7 between the two groups comparatively.

8 So usually we don't worry
9 about this so-called model checking,
10 because there is no model.

11 But anything beyond that,
12 you needed to worry about it. The
13 individual study is a good study or not.
14 You do a meta-analysis at this stage, you
15 have to check. This study is a good
16 paper or not a good paper, right?
17 Everybody is doing now.

18 If it's not a really good
19 paper, you don't include this paper or
20 publication in your meta-analysis, right.
21 That's the practice now.

22 Q. So do you agree that you
23 cannot name one meta-analysis of
24 observational studies that have carefully

1 checked the adequacy of the models of all
2 the studies that were utilized in its
3 analysis?

4 MR. MERRELL: Objection to
5 form.

6 THE WITNESS: You're saying
7 observational studies; is that
8 correct?

9 BY MR. NIGH:

10 Q. Yes.

11 A. No, I don't -- I'm sitting
12 here. I don't know. Maybe I can do some
13 search afterwards and find out for you.

14 Q. It's not the state of the
15 art for published meta-analyses of
16 observational studies to look at each
17 individual study that -- in the
18 meta-analysis and check whether or not
19 all of the studies described adequacy of
20 the models utilized in the analysis,
21 correct?

22 MR. MERRELL: Objection to
23 form.

24 THE WITNESS: Well, sir, I

1 really don't understand. Why do
2 you want to lower your standard?

3 I mean, you have a choice of
4 being very high standard, right?
5 Why do you want to say the
6 majority don't do it, so that's
7 okay and it's acceptable?

8 It's not acceptable.

9 You publish a lot of junk
10 papers in this world, is really
11 not helpful to the society.

12 BY MR. NIGH:

13 Q. Is it your belief that
14 because New England -- you stated
15 multiple times that New England Journal
16 of Medicine no longer publishes
17 meta-analyses.

18 Is it your belief that they
19 are -- that you would give them -- that
20 you ignore them or give them little to no
21 weight?

22 A. Well, they -- I think they
23 got a bad experience from this GSK
24 Avandia study by cardiovascular people in

1 Cleveland Clinic, Steven Nissen. They
2 got really hurt. And the people actually
3 criticized that paper back and forth and
4 left and right. So they feel so
5 embarrassed.

6 So I still remember my old
7 friend, Steve Largaucous, was associate
8 editor, handled that paper for The New
9 England Journal of Medicine. After it's
10 published, I ask Steve, I said, "Steve,
11 how in the world you publish this junk
12 paper?" He said, "Well, I apologize. We
13 didn't realize, you know, the guy used
14 the wrong methodology."

15 Right. Now, they even used
16 the clinical trial data, by the way.
17 It's not observational study. But they
18 used the wrong statistical method to
19 combine in the meta-analysis, right.

20 So everybody jumping up and
21 down. And this is a famous example.

22 Even Congress, you know, had
23 a public hearing. It becomes a really
24 interesting public sort of, like, news,

1 you know, in that days.

2 Anyway, I think New England
3 Journal of Medicine really pissed. They
4 are -- I'm not going to publish any paper
5 in the future using meta-analysis.

6 Q. So is it your belief -- I
7 understand what you're saying about New
8 England Journal of Medicine. Is it your
9 belief that meta-analyses have little to
10 no weight and you would ignore them?

11 A. I don't know why -- I cannot
12 speak for New England Journal of
13 Medicine.

14 If you really wanted to
15 know, I can introduce the editor of New
16 England Journal of Medicine. He's a
17 professor in our school.

18 Q. No, no. I want to make sure
19 you understand my question. I'm not
20 asking about New England Journal of
21 Medicine. Throw that part out.

22 Is it your belief that
23 meta-analyses have little to no weight
24 and you would ignore them?

1 A. If they actually, each
2 individual study, if like we are saying,
3 is very good study, then you can combine
4 information using the so-called
5 well-conducted study, right, as a summary
6 of the so-called group difference.

7 But if you combining, no
8 matter what, the quality of the paper is
9 not very high, and that's really hurting
10 us. Even though you win this legal case,
11 this won't help the society. Right.

12 Q. If a meta-analysis doesn't
13 carefully check the adequacy of the
14 models of every single study that are
15 utilized in the meta-analysis, then you
16 would give that meta-analysis little to
17 no weight and you would ignore it,
18 correct?

19 MR. MERRELL: Objection to
20 form.

21 THE WITNESS: Yeah, I
22 wouldn't take it seriously.

23 BY MR. NIGH:

24 Q. I'm sorry. You said, "Yeah,

1 I wouldn't take it seriously," correct?

2 A. I won't, yeah. I won't take
3 it.

4 Q. Let's take a look at Page
5 13 -- actually Number 12.

6 You can see it starts off
7 with, "In their paper Hidajat, et al.,
8 stated." You can see that Number 24 is
9 talking about Hidajat.

10 On Page 13, you see that,
11 "Censoring" -- middle of the page where
12 it talks about censoring competing
13 events.

14 "Censoring competing events
15 violates the assumption that censoring
16 occurred at random and is independent
17 from the risk of dying from the cause of
18 death of interest, leading to a biased
19 Kaplan-Meier estimator."

20 Do you see that?

21 A. Yes, sir.

22 Q. Is it your belief that the
23 Hidajat study used a Kaplan-Meier
24 estimator?

1 A. No, sir. This is from their
2 paper. It's not my language. I am
3 quoting what they are saying.

4 Q. Yeah. What I'm asking you,
5 is it your belief that the
6 Kaplan-Meier -- that the Hidajat paper
7 utilized a Kaplan-Meier estimator?

8 A. No, no, they tried to avoid
9 using Kaplan-Meier. That's the sentence
10 that you show to us. That's why they
11 don't use Kaplan-Meier. They use
12 cumulative incidence function. These are
13 not my words.

14 Q. Please ex -- Hidajat used
15 the method by Fine and Gray, correct?

16 A. Sorry, say it again.

17 Q. Hidajat used a method by
18 Fine and Gray, correct?

19 A. Oh, yeah. Jason Fine was my
20 student back in Harvard days. You know,
21 he was my Ph.D. student. I know that
22 paper very well.

23 Q. Please explain what the
24 problem is with using the Fine and Gray

1 method?

2 A. You want me to explain to
3 you?

4 Q. Yes.

5 A. Okay. Do you want to go to
6 the paper I cited, the Annals of Internal
7 Medicine. I can take sweet time to
8 explain to you. It's a beautiful paper
9 we wrote.

10 Do you want to do that?

11 Q. Where is the paper that you
12 write about the problems with the Fine
13 and Gray method?

14 A. Go down to reference.

15 Q. I don't see a reference on
16 this page. Is it on the next page?

17 A. Next -- yeah, the next
18 paragraph, 25. We have JAMA-Cardiology,
19 McCaw; New England Journal of Medicine,
20 Annals of Internal Medicine.

21 Those are all papers saying
22 Fine and Gray has a ratio for
23 subdistribution function is not
24 appropriate.

1 You look at the journal we
2 published. New England Journal of
3 Medicine, Annals of Internal Medicine.
4 JAMA-Cardiology. That's really the
5 top -- really top clinical journals,
6 right. It is so hard to get into those
7 journals.

8 As a statistical argument,
9 you can see it. They knew that it was
10 such an important issue. That's why they
11 publish. I'll be more than happy to go
12 through this Internal Medicine paper with
13 you. If you want to go on tomorrow, I'd
14 be happy to spend all day with you.

15 And you are a smart guy.
16 And towards the end of the day, I hope
17 you would support what we are finding,
18 right.

19 Q. I'm not asking you -- I'm
20 not asking to go through the paper. I'm
21 asking you to explain what the problem is
22 with using the Fine and Gray paper. Can
23 you not do that without going through the
24 paper?

1 A. Well, sir, if I say
2 subdistribution function, do you
3 understand what I'm talking about?

4 Q. Yes.

5 A. Well, do you understand what
6 this guy is talking about,
7 subdistribution function?

8 Q. If I'm -- you know, as the
9 attorney, I'm the one who needs to ask
10 you the questions.

11 So I'm asking you, can you
12 explain what the problem is with the Fine
13 and Gray method without utilizing the
14 paper?

15 A. Okay. So let me try. Okay.
16 I guess you don't understand the
17 definition of subdistribution function.

18 So a patient died from
19 cancer, right. And a patient could have
20 died from other causes, cardiovascular
21 events, right. So it's a noncancer
22 death.

23 You have a typical signal
24 illustration. You have two type of

1 death. One is due to cancer. The other
2 one is due to noncancer, right.

3 So this paper is
4 interesting. We said, well, the
5 mortality rate, the overall survival or
6 death rate is 94 percent, is very, very
7 high, almost everybody is dead, right,
8 toward the end of the study.

9 We said, well, the majority
10 of people, they died without a cancer
11 cause. That means people died because of
12 either cardiovascular event or because of
13 kidney failure, whatever you define,
14 right.

15 So you have two types --
16 kinds of death. If the guy says, well,
17 gee, you know, if you guys died from
18 noncancer, I have no idea if the guy
19 survived, how long will it take for him
20 to die from cancer, right.

21 This is what we call
22 competing risk. Right. The two causes
23 are competing with each other. You can
24 observe either one, either die from

1 cancer or die from cardiovascular, right.

2 So I said, well, gee, you
3 know, how do we handle this? So instead
4 of using Kaplan-Meier curve, we started
5 to estimate the distribution of those
6 guys.

7 And I said listen, Counsel,
8 if the guy died from cardiovascular, the
9 reason, right, the cause, what is the
10 this guy's time to die from cancer.

11 I say, man, you know, this
12 guy is already in heaven. I don't know.
13 You know, the guy probably never died
14 from cancer anymore, right. Who knows he
15 didn't have it.

16 So that means if the guy
17 died from noncancer, basically, we have
18 no information about this patient died
19 from cancer anymore.

20 Okay. So that's competing
21 risk.

22 So if you define this
23 cumulative incident curve, which is
24 called subdistribution now because you

1 have the majority of people, they didn't
2 die from cancer.

3 Your distribution never
4 reached one towards the end of the day.
5 Otherwise the subdistribution function
6 should be from zero to one.

7 So that's why we have
8 subdistribution function. Okay.

9 Then you say what is the
10 hazard ratio for this case. I say, wow,
11 gee, well, that's interesting. I'm only
12 interested in the death is due to the
13 cancer. Right. I'm not interested in
14 the death from the non-cancer.

15 I say, well, so how do you
16 define the hazard ratio now?

17 I don't want to -- I don't
18 know, sir -- this is not an insult at
19 all.

20 Do you understand the
21 definition of hazard ratio in general,
22 even without a competing risk, do you
23 understand the definition? Yes or no?

24 Otherwise I can explain to

1 you hazard ratio without a competing risk
2 first.

3 Q. I'm following your answer.
4 But so far I have not heard your
5 explanation of the problem in using the
6 Fine and Gray method.

7 A. Yeah, so obviously you don't
8 understand hazard ratio, right, without
9 competing risk.

10 Hazard ratio is actually is
11 intensity for mortality, force of the
12 mortality. It's not a risk ratio. It's
13 not an odds ratio.

14 So what is the hazard?
15 Hazard means that a person -- and still,
16 for example, six months right now, this
17 guy is still alive.

18 I say, well, gee, you know,
19 Counsel, what is the probability the guy
20 still survive at six months, then
21 suddenly drop dead next week? Okay.

22 And I actually figured out a
23 standardized slope of intensity of this
24 guy what's called hazard. So you go

1 along with six months, 12 months,
2 18 months and et cetera. So you have a
3 curve.

4 That curve is called hazard
5 curve. What is hazard ratio? Hazard
6 ratio means that if -- two groups, they
7 have a two hazard function.

8 And I say what's the hazard
9 ratio? You're assuming these two hazard
10 function are proportional. That means
11 the ratio of the two hazard function is
12 constant over time. You're estimating
13 that parameter. That's why you got the
14 so-called .7, .75, the so-called hazard
15 ratio. Right. Okay. That's for
16 non-competing risk.

17 Then you have a -- there's a
18 competing risk happening. You say, well,
19 gee, you know, I'm only interested in
20 hazard, dying from the cancer. Right.

21 I say okay, so what are
22 you -- what are you talking about now?
23 If a guy die from non-cancer, what are
24 you going to do with the patient?

1 I say, well, I'm going to
2 put a limitation in my risk assess
3 forever. Right.

4 Even the guy died from
5 non-cancer, I said, well, in heaven, the
6 guy is going to eventually develop a
7 death of cancer.

8 Do you think this is a
9 reasonable assumption? Of course not.
10 Right.

11 That's what Jason Fine and
12 Bob Gray's paper, they even themselves
13 indicate it's an interpretation problem.

14 So we actually in the
15 Internal Medicine explain to people, this
16 is paper written for clinical people.
17 You know, it's well written. I recommend
18 it if you cannot falling asleep some
19 night, to pick it up and read it.

20 And we explain to people,
21 this is not logical the quantity you can
22 use. Right.

23 And people didn't know how
24 to do it. So in the Internal Medicine

1 paper, we give alternative ways to help
2 us to understand, instead of using hazard
3 ratio, using something else, right.

4 So that's why people started
5 picking up, oh, yeah, yeah, yeah, this is
6 actually very good.

7 Is that okay with you now?
8 Or you still don't understand?

9 Q. I still haven't heard you
10 explain what the problem is with using
11 the Fine and Gray method.

12 A. I told you. If the guy died
13 from non-cancer, what is the hazard the
14 guy is going to have a cancer death? Can
15 you answer me? No, you can't, right?

16 Jason Fine actually put this
17 guy in the risk assess when they computed
18 the hazard. That's the problem.

19 Q. That's your --

20 A. I don't know if it's too
21 complicated --

22 Q. That's your criticism of the
23 Fine and -- have you -- do you feel like
24 you've given the full answer on your --

1 what you believe to be the problem with
2 using the Fine and Gray method?

3 A. Yeah, you know, this is such
4 complex situation, sir. If you don't
5 read my paper, even I spend 20 minutes
6 with you, I don't think you can get it,
7 right.

8 If you read my paper, just
9 take ten minutes, you can understand the
10 underlying formula. Okay. So, you know,
11 I'd be happy to go through the paper
12 quickly with you if you wanted to, if you
13 really want to find out what's wrong with
14 Jason Fine's estimate.

15 In fact, he wrote this paper
16 asking me to be author. I told him, I
17 say, Jason, this doesn't make sense. And
18 I don't want to be co-author. So he said
19 fine. Okay.

20 Q. Do you feel like you've
21 answered my question on what is the
22 problem with the Fine and Gray method?

23 A. Are you asking me?

24 Q. Yes.

1 A. I said it clearly, but you
2 don't understand. I don't know what I
3 can do.

4 I mean, I said the guy in
5 heaven already, died from a
6 cardiovascular event. And I said how are
7 you computing this guy's hazard for
8 cancer death?

9 Q. Okay. Let's take a look at
10 the next page. Page 14, Number 26.

11 Next you have, "Based on the
12 information available and the content of
13 Dr. Madigan's report, we cannot use the
14 results from diet or occupational studies
15 to make an inference about the exposure
16 effects for the population with
17 valsartan. For example, from the
18 meta-analysis by Song et al., regarding
19 gastric cancer" --

20 A. I'm sorry. Mr. Nigh, could
21 I stop here?

22 Q. You want to take a break?

23 A. Yeah. I'd like to take a
24 break. And we're going to decide we like

1 to continue tonight or not. Is that all
2 right with you?

3 Q. Sure. Yes.

4 MR. MERRELL: Is that all
5 right, Mr. Nigh? We probably
6 should confer. It's going pretty
7 late.

8 THE VIDEOGRAPHER: I'm
9 sorry. Are we going off the
10 record? I'm sorry.

11 MR. NIGH: Definitely.

12 MR. MERRELL: Yes.

13 MR. NIGH: Let's go off the
14 record.

15 THE VIDEOGRAPHER: The time
16 right now is 5:37 p.m. We're off
17 the record.

18 (Excused.)

19 (Deposition adjourned at
20 approximately 5:37 p.m.)

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1
2 CERTIFICATE
3
4

5 I HEREBY CERTIFY that the
6 witness was duly sworn by me and that the
7 deposition is a true record of the
8 testimony given by the witness.

9 It was requested before
10 completion of the deposition that the
11 witness, LEE-JEN WEI, Ph.D., have the
12 opportunity to read and sign the
13 deposition transcript.

14
15 
16

17
18 MICHELLE L. GRAY,
19 A Registered Professional
20 Reporter, Certified Shorthand
21 Reporter, Certified Realtime
22 Reporter and Notary Public
23 Dated: September 17, 2021
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2
3 Please read your deposition
4 over carefully and make any necessary
5 corrections. You should state the reason
6 in the appropriate space on the errata
7 sheet for any corrections that are made.

8 After doing so, please sign
9 the errata sheet and date it.

10 You are signing same subject
11 to the changes you have noted on the
12 errata sheet, which will be attached to
13 your deposition.

14 It is imperative that you
15 return the original errata sheet to the
16 deposing attorney within thirty (30) days
17 of receipt of the deposition transcript
18 by you. If you fail to do so, the
19 deposition transcript may be deemed to be
20 accurate and may be used in court.

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PAGE LINE CHANGE

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1
2 ACKNOWLEDGMENT OF DEPONENT

3
4 I, _____, do
5 hereby certify that I have read the
6 foregoing pages, 1 - 401, and that the
7 same is a correct transcription of the
8 answers given by me to the questions
9 therein propounded, except for the
10 corrections or changes in form or
11 substance, if any, noted in the attached
12 Errata Sheet.

13
14
15 _____
16 LEE-JEN WEI, Ph.D.

DATE

17
18
19 Subscribed and sworn
to before me this

20 _____ day of _____, 20____.

21 My commission expires: _____
22 _____

23 Notary Public
24

1	LAWYER ' S NOTES		
2	PAGE	LINE	
3	_____	_____	_____
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